YNTHESES OF SOME HETEROCYCLES USING CHLOROSULFONYL ISOCYANATE, ENAMINES, DIAZOMETHANE, 1,3-DIPHENYL-NITRILIMINE AND CERIC AMMONIUM NITRATE

A Thesis Submitted

In Partial Fulfillment of the Requirements

for the Degree of

DOCTOR OF PHILOSOPHY

by

MANISHA TRIPATHI

to the

DEPARTMENT OF CHEMISTRY

INDIAN INSTITUTE OF TECHNOLOGY KANPUR

AUGUST, 1986

Dedicated

to

My Beloved Parents

Nor Art, nor power, nor to:

The measure of the Eternal

Nor hymn, nor prayer, nor

STATEMENT

I hereby declare that the matter embodied in this thesis is the result of investigations carried out by me in the Department of Chemistry, Indian Institute of Technology, Kanpur, India, under the supervision of Professor Durga Nath Dhar.

In keeping with the general practice of reporting scientific observations, due acknowledgement has been made wherever the work described is based on the findings of other investigators.

MANISHA TRIPATHI

Kanpur:
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CERTIFICATE OF COURSE WORK

This is to certify that Miss Manisha Tripathi has satisfactorily completed the following courses required for the Ph.D. degree programme.

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Chm 505	Principles of Organic Chemistry
Chm 541	Advanced Inorganic Chemistry
Chm 581	Basic Biological Chemistry
Chm 614	Organic Photochemistry
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Certified that the work embodied in this thesis entitled: "SYNTHESES OF SOME HETEROCYCLES USING CHLOROSULFONYL ISOCYANATE, ENAMINES, DIAZOMETHANE, 1,3-DIPHENYLNITRILIMINE AND CERIC AMMONIUM NITRATE" has been carried out by Miss Manisha Tripathi under my supervision and the same has not been submitted elsewhere for a degree.

D. N. Dhar

(Durga Nath Dhar)
Thesis Supervisor

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August 1986.

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PREFACE

The thesis comprises of four chapters. Chapter I has been divided into Part A and Part B. Part A highlights the reactions of various substituted 4 phenyl thiosemicarbazones, 4 aryl semicarbazones, keto schiffs bases and 2,3-diphenyl-5,6-dihydro pyrazine with chlorosulfonyl isocyanate (CSI). Part B describes the reactions of various flavanones with chlorosulfonyl isocyanate. CSI, the versatile heterocumulene is known to be one of the most active isocyanates. Its reactions as an uniparticulate electrophile has expanded the horizon of heterocyclic chemistry. In an attempt to widen the scope of such reactions and to understand the nature of reaction of CSI with various compounds containing C=N group, investigations were carried out on the reactions of this active reagent with 4 aryl thiosemicarbazones,4 aryl semicarbazones, keto schiffs bases and 2,3-diphenyl, 5-6-dihydro pyrazine.

The 4 aryl thiosemicarbazones used in the investigation include acetone 4 aryl thiosemicarbazone (1a), ethyl-methyl ketone 4-aryl thiosemicarbazone (1b), cyclohexanone-4-phenyl-thiosemicarbazone (1c), cyclopentanone-4-phenyl-thiosemicarbazone (1d), diethyl ketone 4-phenyl-thiosemicarbazone (1e). The other compounds which were taken up for our study include 4-p-chlorophenyl substituted thiosemicarbazones of acetone (1f), ethyl-methyl ketone (1g), cyclohexanone (1h), cyclopentanone (1i),

diethyl ketone (1j) and 4-bromophenyl thiosemicarbazone of acetone (1k). The cyclisation of 4-phenyl thiosemicarbazones was found to take place with loss of SO_2 to furnish 4-phenyl Δ'-[1,2,4]-triazoline-5-thiones (5a-k). The reactions were carried out by adding equivalent amount of CSI to (1a-k). Reaction of benzophenone 4-phenyl semicarbazone with CSI afforded benzophenone and heterocyclic system (9). The Ketoschiffs bases react with CSI to yield the corresponding keto compounds in quantitative yields. The ketimines employed in the study include triphenyl imine, diphenyl-N-toluyl ketimine, dibenzil ketimine, fluorene ketimine, α-naphthyl-phenyl-ketimine, phenyl-methyl, phenyl ketimine, isobutyl-methyl,phenyl ketimine and ethyl-dimethyl, ketimine. Reaction of 2,3-diphenyl-5,6-dinydro pyrazine with CSI afforded benzil. The structures of all these compounds were assigned on the basis of spectroscopic and analytical data.

In Part B (Chapter I) are described the reaction of CSI with oxygen heterocycles viz., flavanones. The flavanones taken up for our investigations include flavanone, 4-methyl flavanone, 4'-methoxy flavanone and 3',4'-dimethoxy flavanone. The usual site of attack by the CSI is the C_3 position of the flavanone molecule. CSI reacts to furnish two different classes of heterocyclic systems: (109-112) and (113-116) respectively.

In Chapter II-A are highlighted the reactions of various substituted 4-styryl-1,2,3-benzoxathiazine-2,2-dioxides (1a-f) with enamine. The investigations carried out on the addition reaction of diazomethane with the aforesaid compounds are dealt with in Part B of the second chapter.

4-Styryl-1,2,3-benzoxathiazine-2,2-dioxides contain C=C and C=N groups in conjugation. The presence of SO_2 moiety in these compounds (1a-f) makes them an electron-deficient hetero-diene system. In an attempt to expand the horizon of hetero-cyclic chemistry, the reactions of (1a-f) with various enamines were carried out. The five enamines employed in the present investigation include, 1-pyrrolidino-1-cyclohexene (2), 1-piperi-dino-1-cyclohexene (3), 1-pyrrolidino-1-cyclopentene (7), 1-mor-pholino-1-cyclohexene (6) and 1-piperidino-1-cyclopentene (8). Out of the five enamines employed, the reactions of 1-pyrrolidino-1-cyclohexene (2) and 1-piperidino-1-cyclohexene (3) with (1a-f) are most interesting. These reactions constitute a versatile method for the syntheses of the novel bridged heterocyclic systems (4a-f) and (5a-f). The participation of the solvent, molecule, acetonitrile, has been postulated in these reactions. The structures of the products were confirmed by spectroscopic and analytical data. Other enamines viz., 1-pyrrolidino-1-cyclo-pentene (7), 1-morpholino-1-cyclohexene (6) and 1-piperidino-1-cyclopentene (8) have been found to undergo [4+2] cyclo-addition

reaction with (1a-f), to afford the heterocyclic systems (9a-f), (10a-f), (11a-f) respectively. The reactions of dichloro-ketene with (1a) has been found to furnish the heterocyclic system (12) by [2+2] addition across the C=N of (1a). Diazomethane, a 1,3-dipole, has been found to add across the C=N moiety of these heterocyclic systems (1a-f) to yield a new class of heterocyclic system (3a-f). The mass fragmentation pattern points to the fact that one molecule of diazomethane has been added up during this reaction.

Studies on the reactions of 1,2,3-benzoxathiazine-2,2-dioxides with 1,3-diphenyl nitrilimine forms the subject matter of Chapter III. The benzoxathiazine-2,2-dioxides taken up for ou investigation include 1,2,3-benzoxathiazine-2,2-dioxide (a), 4'-chloro-1,2,3-benzoxathiazine-2,2-dioxide (b), 2',6'-dichloro-1,2,benzoxathiazine-2,2-dioxide (c), 4'-methoxy-1,2,3-benzoxathiazine 2,2-dioxide (d), and 2',6'-dimethoxy-1,2,3-benzoxathiazine-2,2-dioxide (e). The 1,3-dipolar cyclo-addition offers a vast scope in the syntheses of a wide variety of heterocyclic compounds, which can not be accomplished so easily by other means. Reaction of benz-N-phenylhydrazidoyl chloride with (3) resulted in the formation of a novel heterocyclic system (5a-g). 1,3-diphenyl-nitrilimine (generated *in situ*) adds to the C=N group of these compounds. The structure of these compounds were confirmed by spectroscopic and analytical data.

Chapter IV highlights the ceric ammonium nitrate (CAN) oxidation of various substituted 4-phenyl-Δ'-[1,2,4]triazoline-5-thiones, 3H-1,2-benzodithiole-3-thiones and flavanones. The study of the oxidation of 4-phenyl-Δ'-[1,2,4]triazoline-5-thiones with pyridinium chlorochromate (P.C.C.) also forms the subject matter of this chapter. CAN has been found to be an efficient oxidant for 4-phenyl-Δ'-[1,2,4]triazoline-5-thiones. The thiones chosen for the study include 3,3-dimethyl-4-phenyl-Δ-[1,2,4]-triazoline-5-thione (5a), 3-ethyl, 3-methyl-4-phenyl-Δ'-[1,2,4]-triazoline-5-thione (5b), cyclohexane spiro-3'-(4'-phenyl-Δ'-[1',2',4']triazoline thione) (5c), cyclopentane spiro-3'-(4-phenyl-Δ'-1',2',4']triazoline-5'-thione) (5d) and 3,3-diethyl-4-phenyl-Δ'-[1,2,4]triazoline-5-thione (5e). Other triazoline thiones taken up for the present investigation are various 4-p-chloro-phenyl substituted thiones (5f-j). In all these cases CAN converted these thiones into their corresponding triazoline-5-ones (327a-j) in excellent yields. This conversion method is mild and provides a versatile alternative method for the preparation of triazolinones. In addition, the reaction of CAN with 3H-1,2-benzodithiole-3-thiones furnish their corresponding benzodithiole-3-ones. The substrates taken up for the present investigation include 3H-1,2-benzodithiole-3-thione , 5-CH_3, 3H-1,2-benzodithioles , 7-CH_3, 3H-1,2-benzodithiole , 5,7-dichloro- and 5-chloro-3H-1,2-benzodithiole 3-thiones. Studies on the oxidation reactio

of CAN was extended to various substituted flavanones. Flavanones are found to be cleaved by CAN to afford a new class of heterocyclic compounds. The flavanones used for this study include flavanone, 4-methyl flavanone, 4'-methoxy flavanone and 3'-4'-dimethoxy flavanone. In all these compounds the nitrato compounds (333a-d) were obtained.

Pyridinium chlorochromate (P.C.C.) has been found to be an efficient oxidant for the conversion of 4-phenyl-Δ'-[1,2,4]-triazoline-5-thiones into their corresponding triazoline-5-ones.

CONTENTS

..contd.

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CHAPTER I-A

REACTION OF CSI WITH 4-ARYLTHIOSEMICARBAZONES, 4-ARYLSEMICARBAZONES, KETO SCHIFFS BASES AND 2,3-DIPHENYL-5,6-DIHYDROPYRAZINE

With a view to enlarge our understanding about the addition reaction of CSI, we became interested to study the reaction of this reagent with compounds containing carbon-nitrogen double bond. In this context we selected 4-aryl semicarbazones and 4-aryl thio-semicarbazones, keto-schiffs bases and 2,3-diphenyl-5,6-dihydro pyrazine as the suitable substrates. It turned out that the reaction of 4-aryl thiosemicarbazones with CSI led to the exclusive formation of a novel heterocycle (5a-k), while 4-aryl semicarbazon produced a cleavage product, a ketone and the heterocyclic system (9a-f). In the latter cases, the cleavage reaction was favoured. An alternative method, for the synthesis, of heterocyclic system (5a-k), is, however, available in the literature and is based on the oxidative cyclisation of 4-substituted thiosemicarbazones,

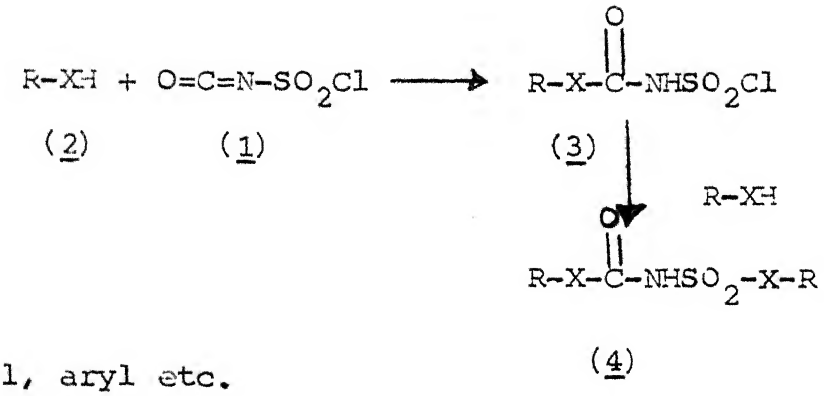
brought about under the influence of basic alumina. The reaction is described to take a long time (90 hours).

The reaction of the versatile electrophile chlorosulphonyl isocyanate with various 4-aryl-thiosemicarbazones have been studied. It has been found that CSI reacts, at room temperature, with thiosemicarbazones, with the formation of the novel heterocyclic systems viz., Δ'-[1,2,4]triazoline-5-thiones. There is only one method reported in literature for the synthesis of these heterocyclic systems and is based on the oxidative cyclisation[1] of 4-substituted thiosemicarbazones brought about under the influence of basic alumina. The method reported by us for the synthesis of Δ'-(1,2,4)triazoline-5-thione has several advantages over that described in literature. Thus, the reaction takes place under mild conditions, in a shorter period of time, and furnishes the product in an excellent yield. The experiment involves the addition of equivalent amount of CSI to a stirred solution of 4-aryl thiosemicarbazones at 0°, and the desired product, in a high state of purity is isolated in the usual way.

INTRODUCTION

Chlorosulfonyl isocyanate (CSI) discovered by Graf[2,3] in 1952 is the most reactive isocyanate known. The polar chlorosulfonyl group attached to the cumulative double bond in CSI, enhances the reactivity of isocyanate group such that the carbon

Scheme I.1

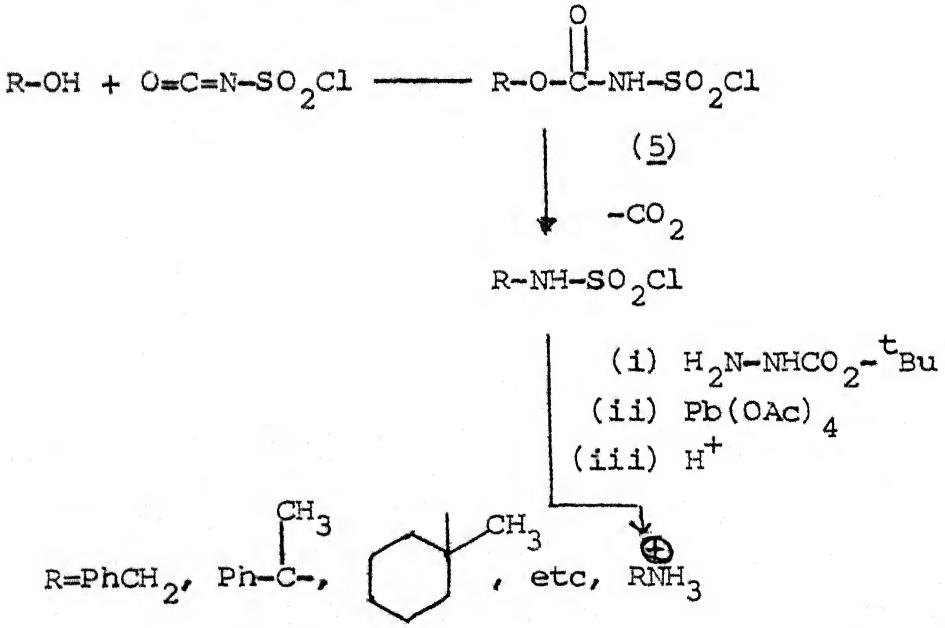


R=H, alkyl, aryl etc.

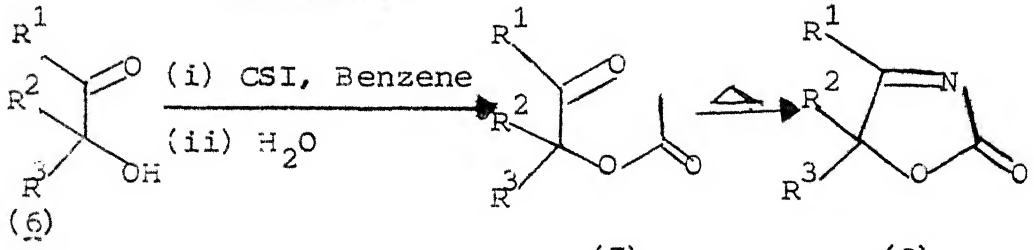
X=O, NH, NR', S.

The facile reactions of CSI with alcohols have been exploited in their conversion to the corresponding amines[12]. This mainly applies to tertiary and benzylic alcohols, ROH, in which the alkyl portion R is able to support a positive charge (Scheme I.2). A simple synthesis of oxazolidones[13] is possible by the reaction of CSI with α-keto alcohols (Scheme I.3).

Scheme I.2



Scheme I.3



(6) (7) (8)

R^1=Ph, t-Bu

R^2, R^3=Me, Pn

The exceptional reactivity of CSI with alcohols makes its possible to derivatize primary alcohols in the presence of other functionalities. This has been utilized in the synthesis[14,15] of (±)-I- carba analogues of cefoxitin (10) (Scheme I.4).

The reaction of phenols with CSI, at ordinary temperatures, is quite analogous to that of alcohols. But at elevated temperature the reaction affords a new class of reactive isocyanate, viz. aryloxysulfonyl isocyanate (13), which on hydrolysis yield aryl esters[16] of sulphamic acid (14) (Scheme I.5).

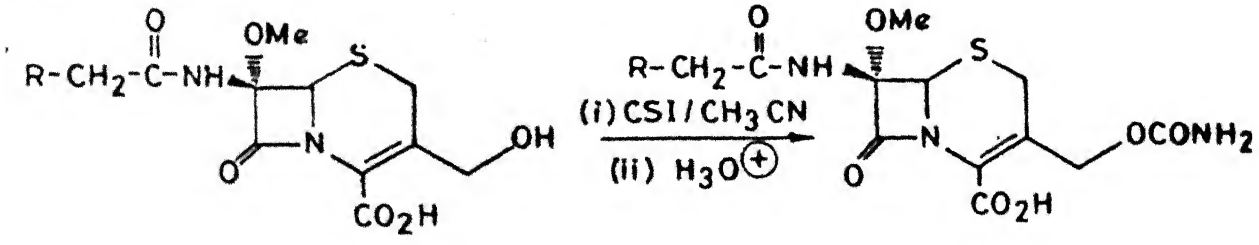
Salicylaldehydes and o-hydroxyacetophenone react[17] with CSI, at room temperature, to give benzoxazinones (15). The same reaction, in refluxing toluene, affords 1,2,3-benzoxathiazine-2,2-dioxides (16)[18] in good yields.

Similarly, CSI reacts with catechols to give a new family of seven membered heterocycles, viz., the benzo-(f)-2,2,4-trioxo-1,5,2,3-dioxathiazepins (17)[19].

R^1 = ph, t-Bu

R^2, R^3 Me, ph

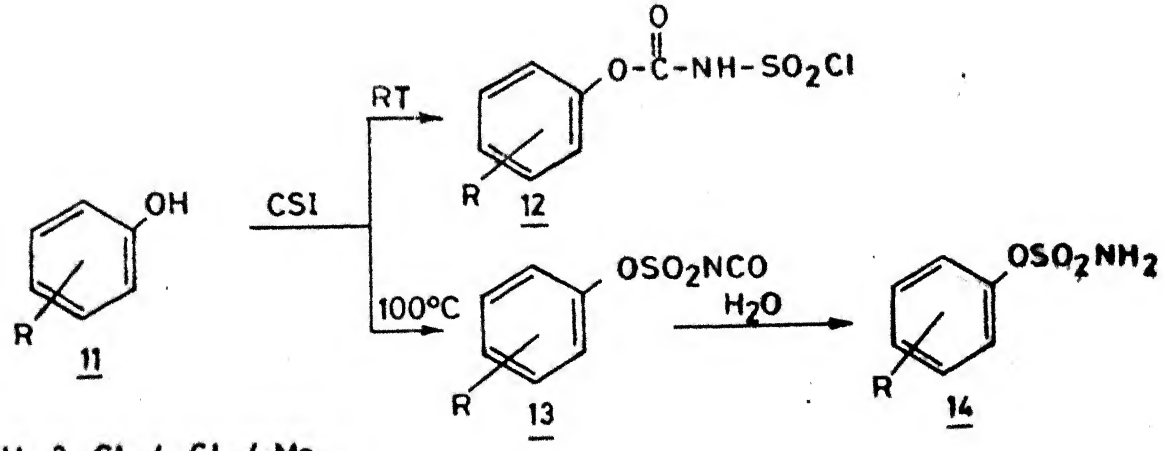
SCHEME 1.4



9 10

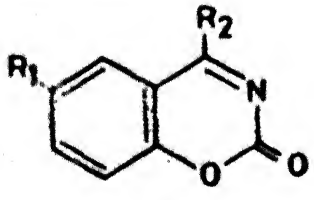
R = 2-thienyl

SCHEME 1.5



11 12 13 14

R = H, 3-Cl, 4-Cl, 4-Me, 4-OMe, 4-CN



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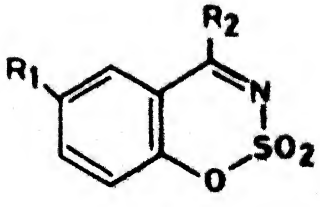

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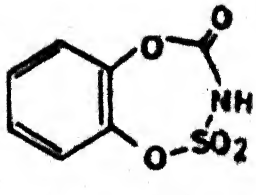

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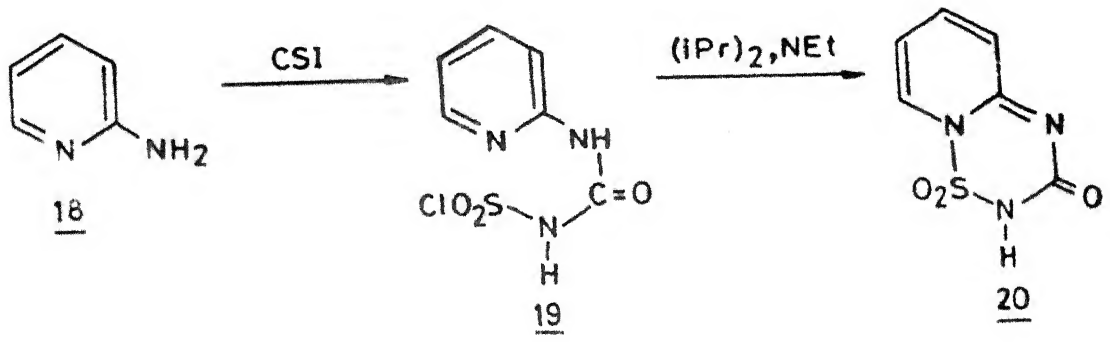
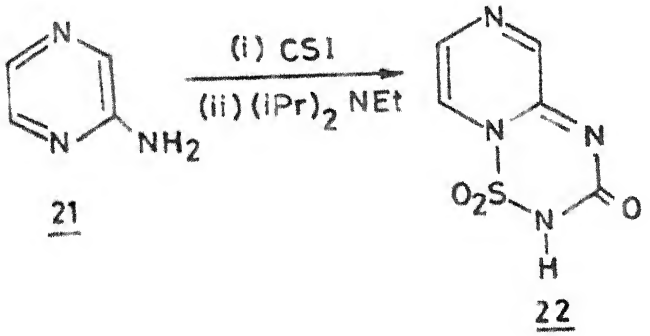
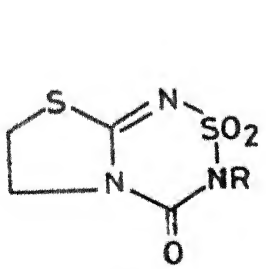
SCHEME 1.6







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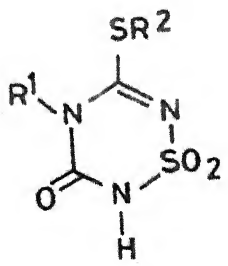

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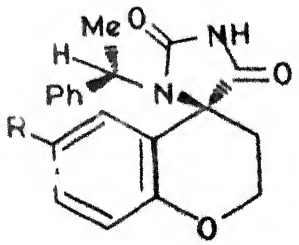
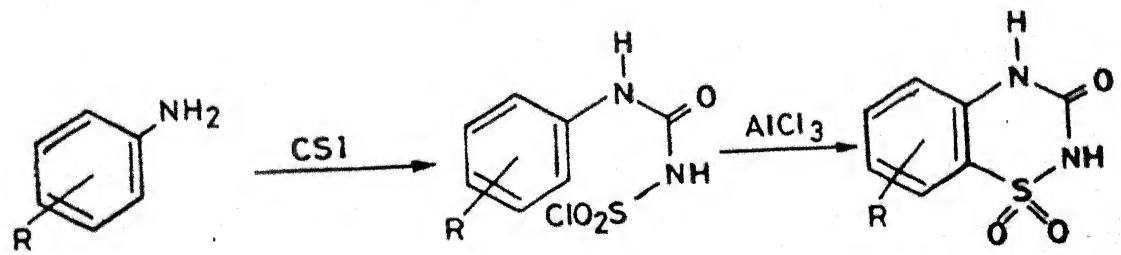


25 R = Cl, F

SCHEME 1.7



R = H, 4-Me, 2-Me, 4-Cl, 3-Br, 4-OMe.

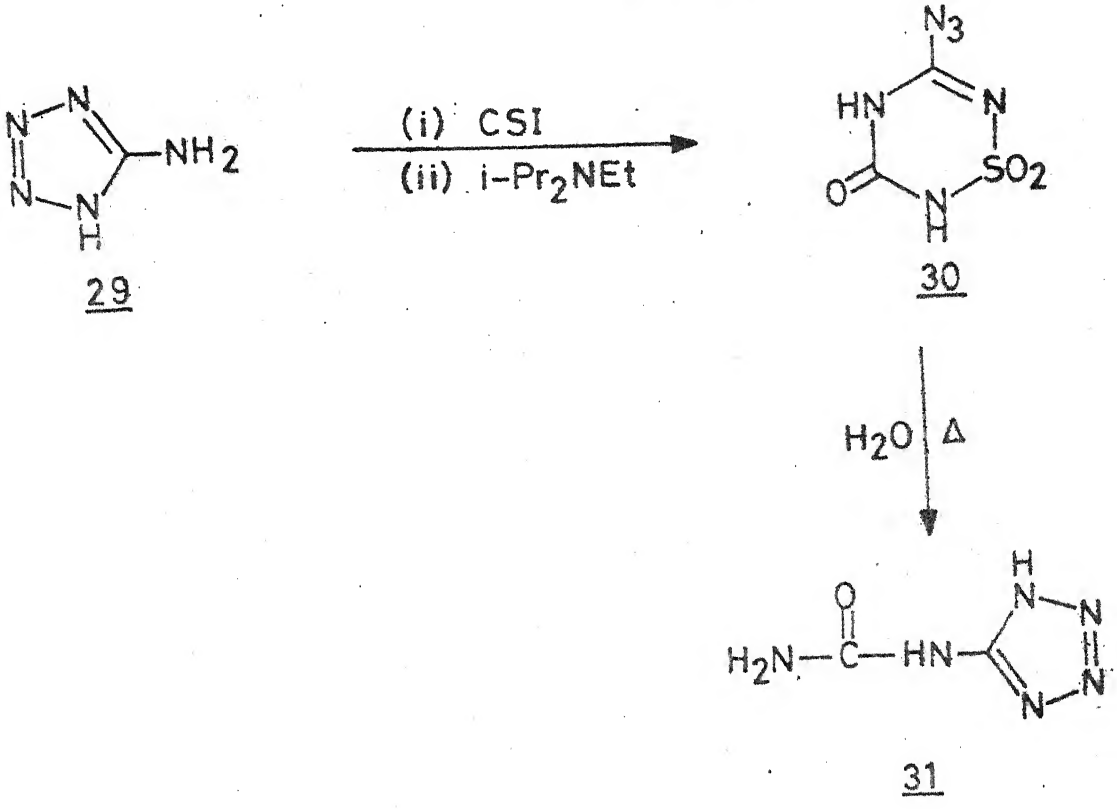
The facile reaction of CSI with amines has been exploited in the syntheses of some heterocyclic compounds, Karady et al.[20] have reported the reaction of CSI with 2-amino-pyridine (18) and 2-aminopyrazine (21). The intermediate (19) formed in this reaction, undergoes smooth cyclization in the presence of ethyl diisopropylamine to give the triazine (20) (Scheme I.6). Likewise, thiatriazine derivatives (23) and (24) can be prepared by the reaction of isothioureas with CSI[21]. Sterically hindered C-amino nitriles react with chlorosulfonyl isocyanate to give, after hydrolysis, the corresponding hydantoins (25)[22]. This has been utilized in the syntheses of optically active spirohydantoins.

A new synthesis of 1,2,4-benzothiadiazines (28) has been achieved by the reaction of aniline and substituted anilines with CSI, followed by a Friedel-Crafts cyclization[23] (Scheme I.7).

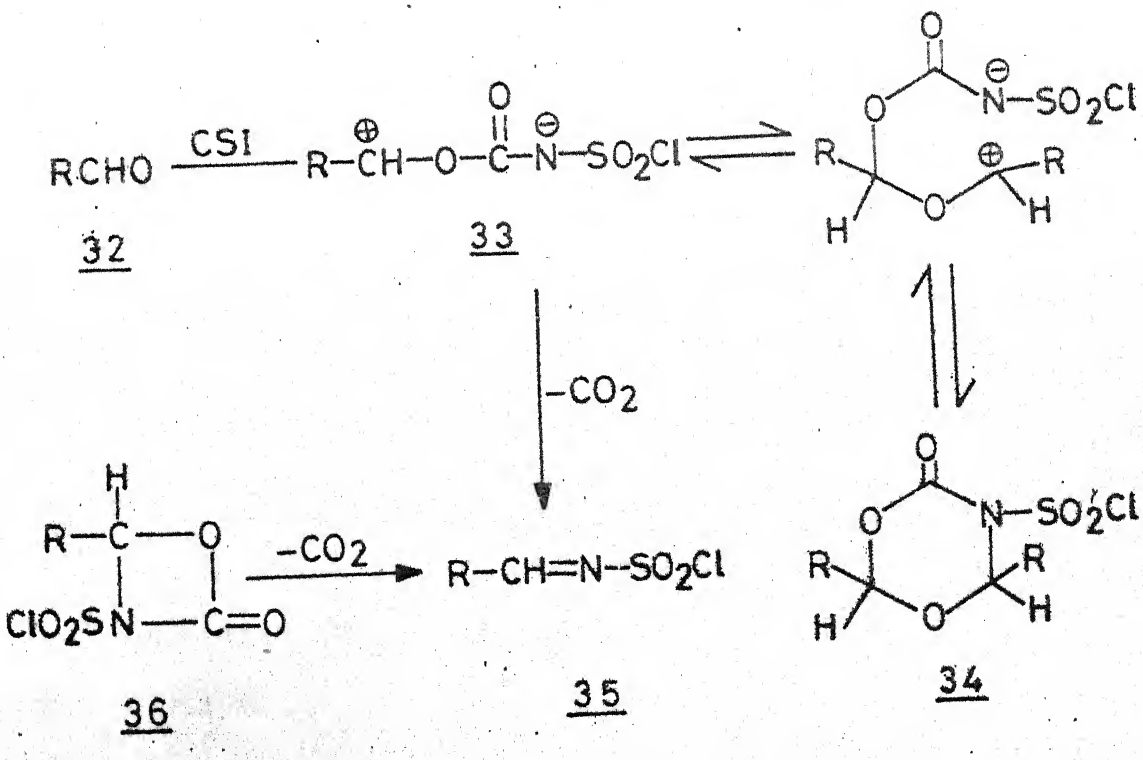
The reaction of CSI with 1H, tetrazol-5-amine (29)[24] and subsequent treatment with a hindered base, ethyl diisopropylamine, affords an interesting thiatriazine derivative (30). Brief treatment of (30) with boiling water converted it into the urea (31) in which the tetrazol system was reconstituted (Scheme I.8). Recently Olah et al.[25] have used CSI in converting aldoximes and amides into nitriles, thus employing it as a dehydrating agent.

Carboxylic acids react readily with CSI, to form a relatively unstable intermediate, which then loses carbon dioxide to give

Scheme I.8



Scheme I.9



the corresponding N-chlorosulfonyl carboxamides[26]. These carboxamides can in turn be converted, in situ to nitriles in good overall yields, by treatment with dimethyl formamide. Chlorosulfonyl isocyanate has been found to be good reagent for the conversion of carboxylic acids to the corresponding anhydrides, amides and esters[27]. Both aliphatic and aromatic carboxylic acids have been found to undergo smooth transformation in the presence of carboxylic acids, aliphatic and aromatic amines, alcohols and phenols to give the corresponding anhydrides, amides and esters in good yields.

Reactions with carbonyl compounds

The cycloaddition of sulfonyl isocyanates across carbon oxygen double bond in aldehydes and ketones is a useful method for the synthesis of sulfonyl-imines. Graf[28] has reported, the formation of N-chlorosulfonylazomethine, when CSI reacts with aldehydes, at room temperature. The azomethines derivative may be considered to be formed from [2+2] cycloaddition product, followed by loss of carbon dioxide. On the basis of spectroscopic methods it has been shown, that at low temperature, CSI reacts with benzaldehyde and acetaldehyde (molar ratio 1:2) to give the corresponding derivatives of dioxazines (34)[29] (Scheme I.9).

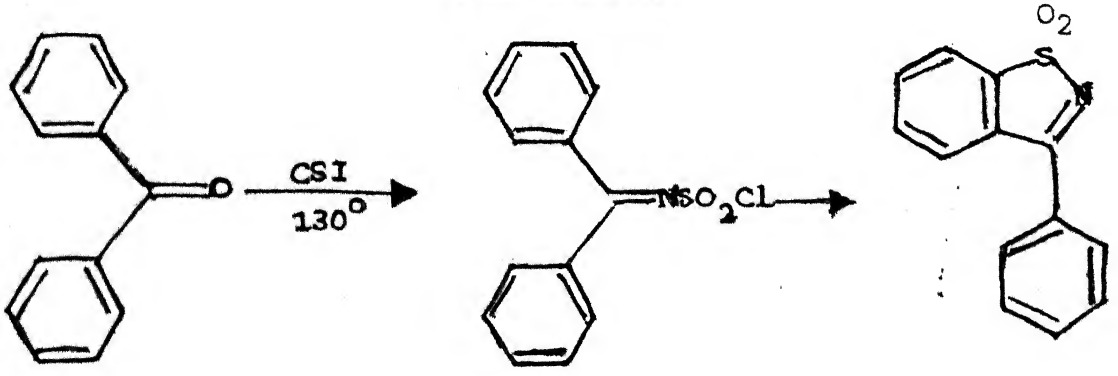
The formation of (34) favours the intermediacy of the 1,4-dipolar species (33). However, the exact rate of carbon-nitrogen bond formation in relation to carbon dioxide elimination is

difficult to determine and therefore, the transient formation of the oxazetidinone (36) can not be ruled out (Scheme I.9).

The reaction of CSI with ketones is, however, more complicated. The reaction products with different structural features have been isolated, depending upon the structures of ketones, concentration of the reactants and the experimental conditions employed.

Equimolar reaction of CSI with 1,2-diphenyl cyclopropane[30], tropone[31], 2,6-diphenyl-4(H)-pyran-4-one[32] and flavone[32] led to the formation of the corresponding iminesulfonyl chlorides. Benzophenone reacts with CSI, at elevated temperature, to form benzothiazole-1,1-dioxide, via the intermediate azomethine[29] (Scheme I.10).

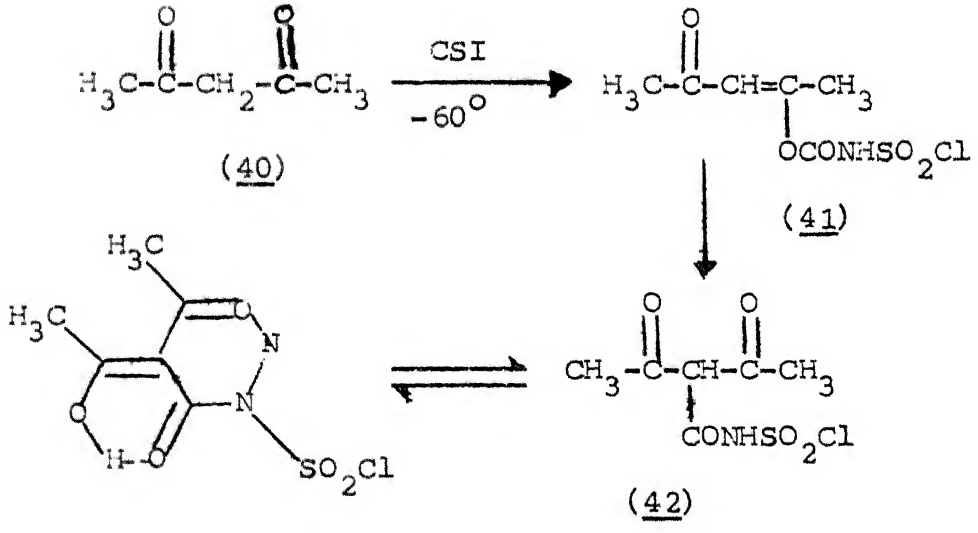
SCHEME I·10



(37) (38) (39)

Acetyl acetone, reacts with CSI to produce the enol carbamate (41) in 87% yield, at low temperature. The compound (41), rearranges, on warming the solution, to (42), via an elimination reaction and re-addition of CSI (Scheme I.11)[29]. β-Carboxamide (42) is, however, formed when the above reaction is carried out at room temperature.

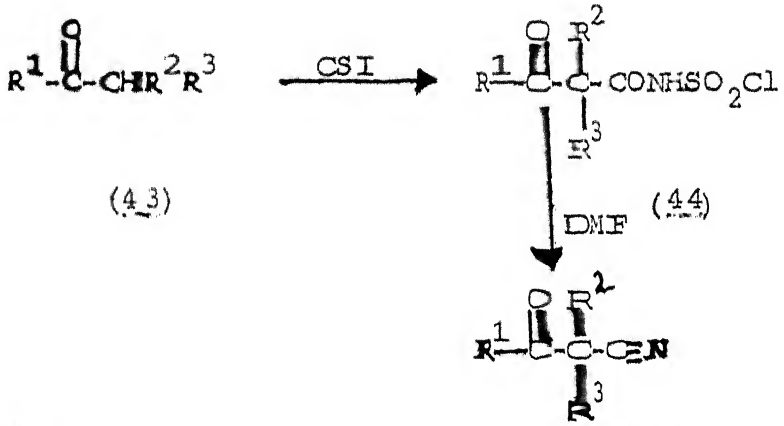
Scheme I.11



Enolizable ketones undergo electrophilic reaction with CSI to produce N-chlorosulfonyl-β ketocarboxamides (44)[29,33]. These compounds can be converted, by treatment with DMF, into the corresponding β-ketonitriles (45) in high yields (Scheme I.12)[34]. Under appropriate conditions, β-keto-amides (46) obtained from aliphatic and aromatic ketones, can undergo further transformation.

This involves a second electrophilic addition of CSI to the enol tautomer, to produce malonamide derivative (48). Hassner and Rasmussen reported[35], for the first time, the electrophilic addition of CSI to simple ketones, which provides a facile entry into the 3,4-dihydro-4-oxo-1,2,3-oxathiazine-2,2-dioxide (50) and 3,4-dihydro-2H-2,4-dioxo-1,3-oxazine (52). When ether is used as a solvent, CSI acting as a Lewis acid[36], can abstract a chloride ion from (46) thus producing (49) which in turn gives (50) by a proton transfer and ring closure.

Scheme I.12



(43) (44) (45)

R^1=C_6H_5, C_2H_5, CH_3

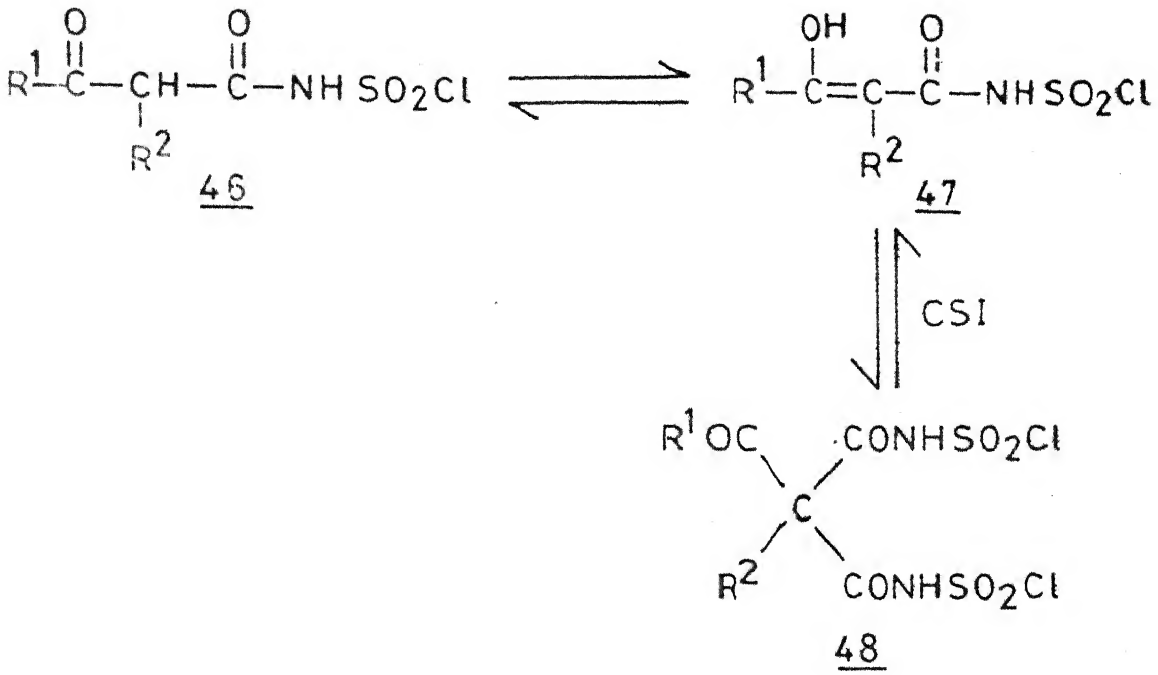
R^2=C_2H_5, CH_3, $COCH_3$

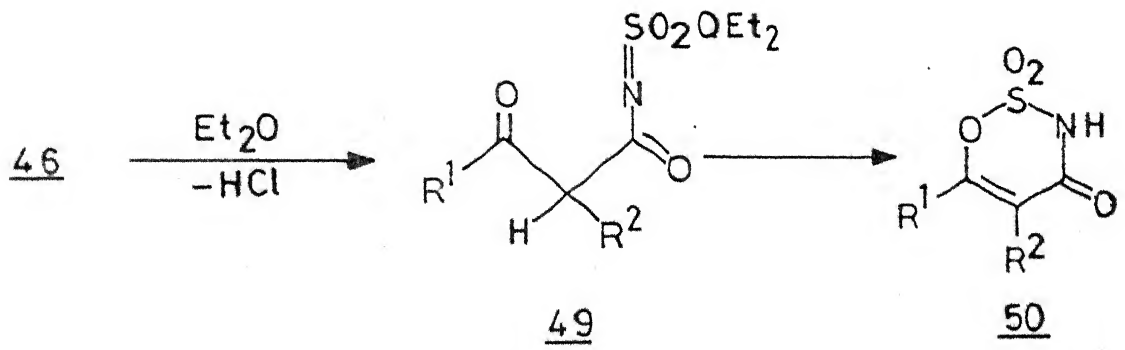
R^3=H, CH_3

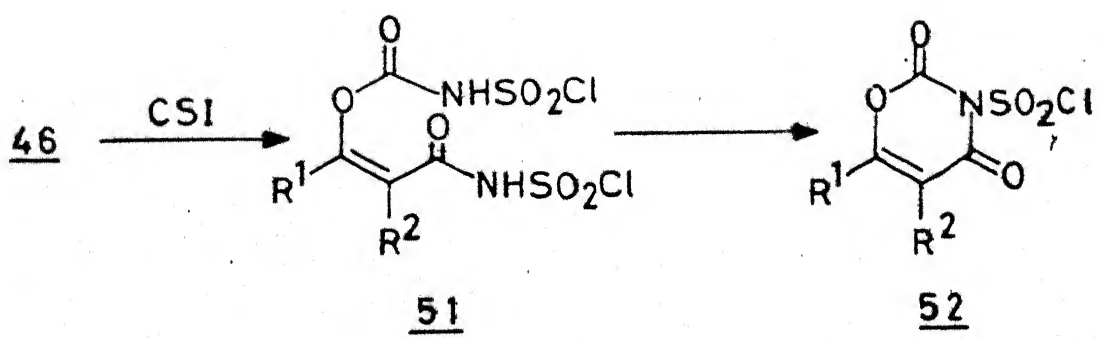
63-90%

CSI reacts with (47) to produce enol carbamate (51) and this cyclizes with loss of sulphamoyl chloride to furnish (52), in fairly good yields (Scheme I.13).

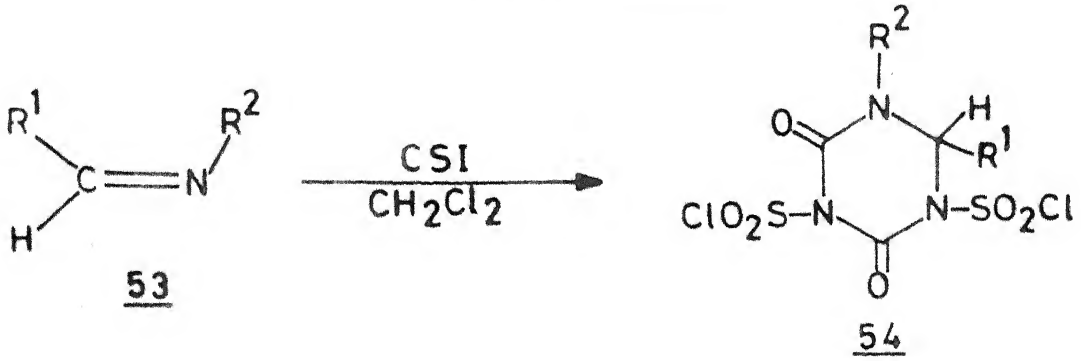
Scheme 1.13



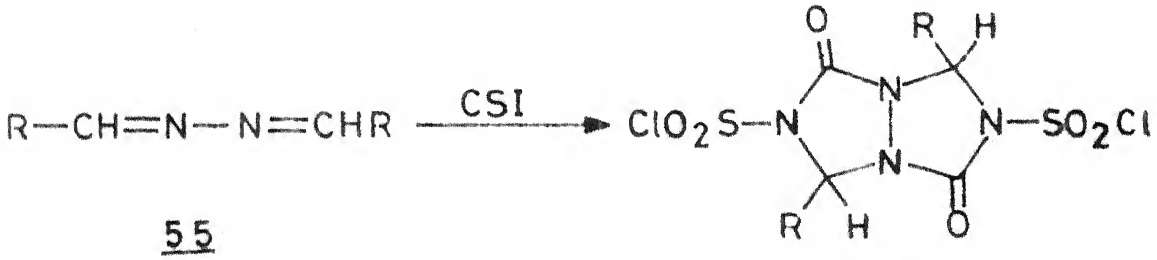




Scheme 1.14

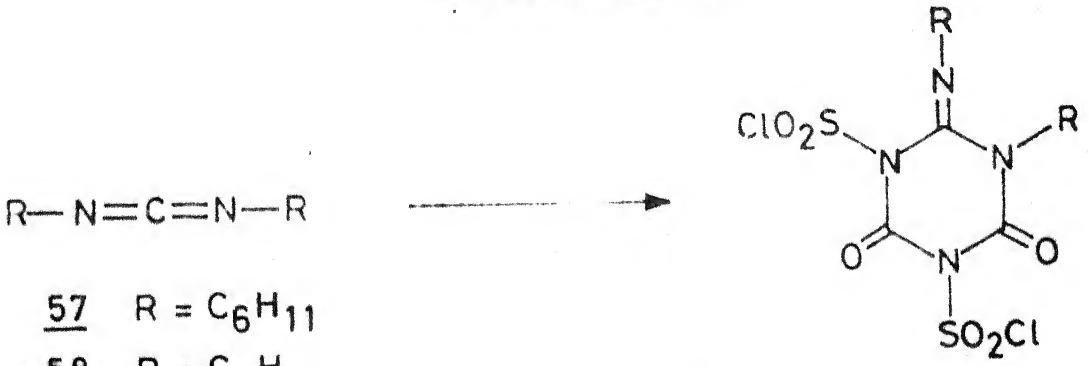


53 54



55 56

Scheme 1.15

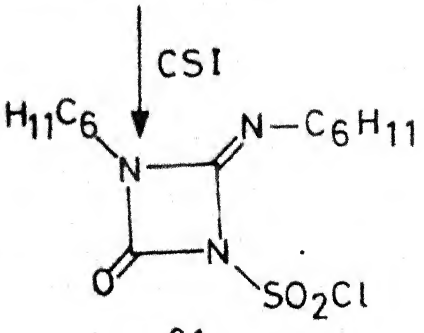


57 R = C_6H_{11}

58 R = C_6H_5

59 R = C_6H_{11}

60 R = C_6H_5



61

Reactions with carbon nitrogen bonds:

Suschitzky et al.[37] have made a detailed investigation on the reaction of CSI, with carbon nitrogen double bonds. Schiff's bases react with CSI in a 1:2 molar ratio to produce triazine-diones, whereas azines (which can be regarded as bis - anils) react with CSI to give tricyclic tetraza-compounds (56) (Scheme I.14).

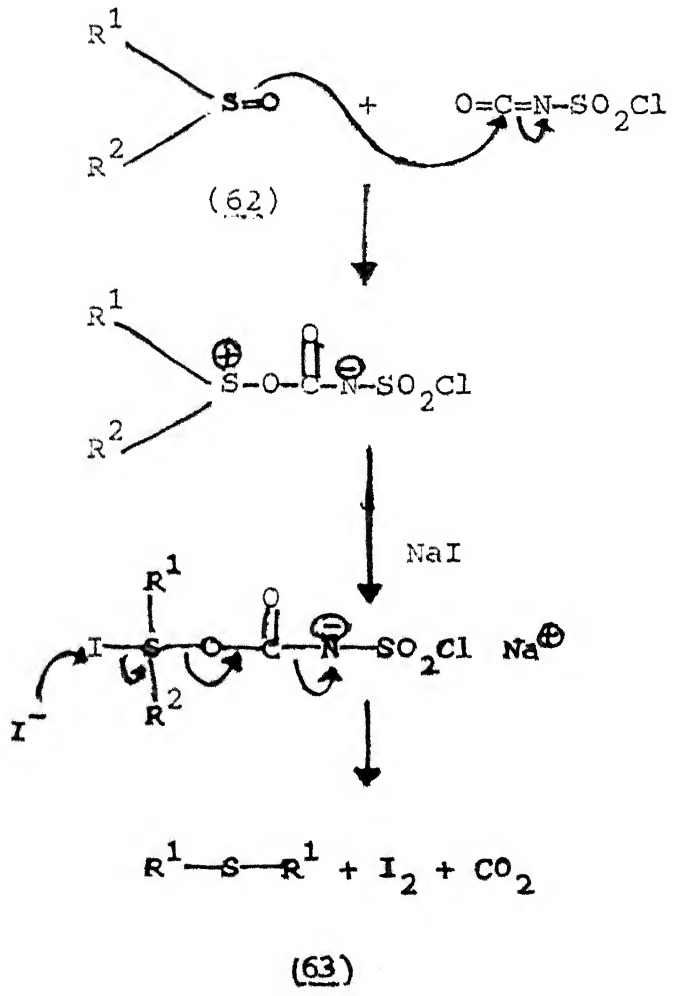
The dropwise addition of CSI to the diimide (57) is reported[37] to yield the diazetidinone (61), while the inverse addition a 2:1 CSI - diimide adduct triazinedione (59) was obtained. However, it is interesting to note that diphenyl carbodiimide (58) gave triazinedione (60), regardless of the mode of addition[37] (Scheme I.15).

Reaction with sulfur oxygen double bonds:

Dimethyl sulfoxide reacts with CSI at low temperature, to form N-chlorosulfonyl dimethyl sulfimide[6], by the elimination of carbon dioxide from the initially formed CSI-DMSO adduct.

Keshavmurty et al.[38] have found that CSI/NaI reagent system to be very efficient for the reduction of sulfoxides to sulfides (Scheme I.16).

Scheme I.16

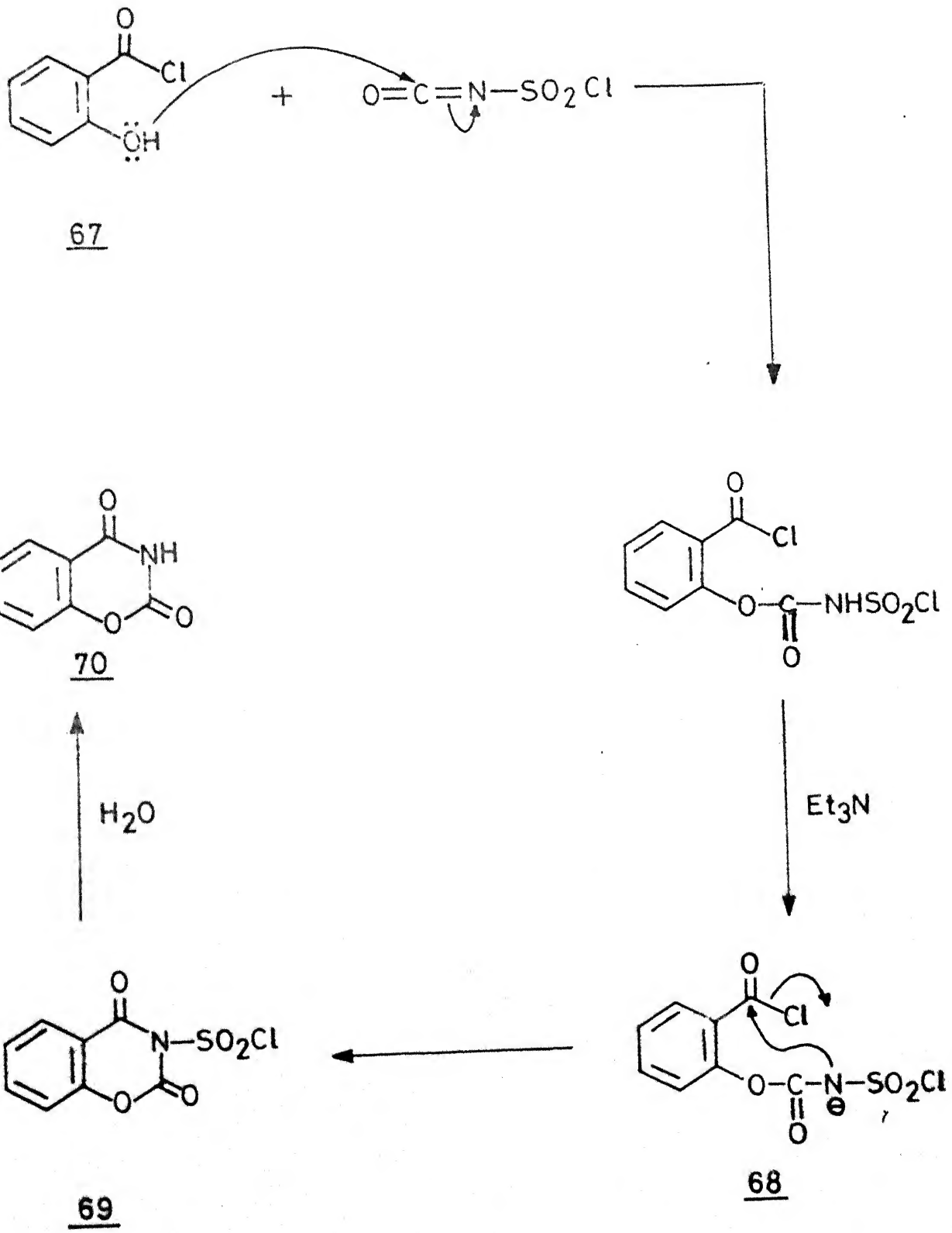


(62)

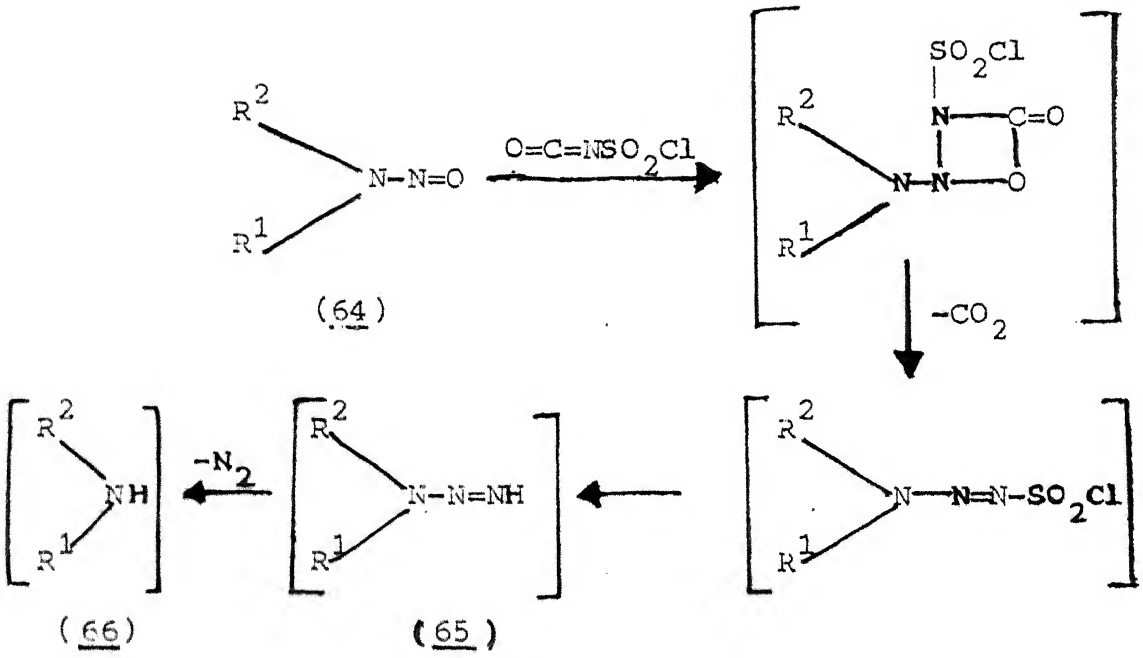
(63)

Bag et al.[39] have studied the reaction of CSI with nitrosamines. According to the authors, this reaction provides a milder method for the conversion of nitrosamines to aliphatic secondary amines (Scheme I.17).

Scheme 1.18


O
Cl
OH
+
O=C=N—SO2Cl
67
O
Cl
O—C—NHSO2Cl
O
Et3N
68
O
Cl
O—C—N—SO2Cl
Θ
O
N—SO2Cl
O
O
69
H2O
O
NH
O
O
70

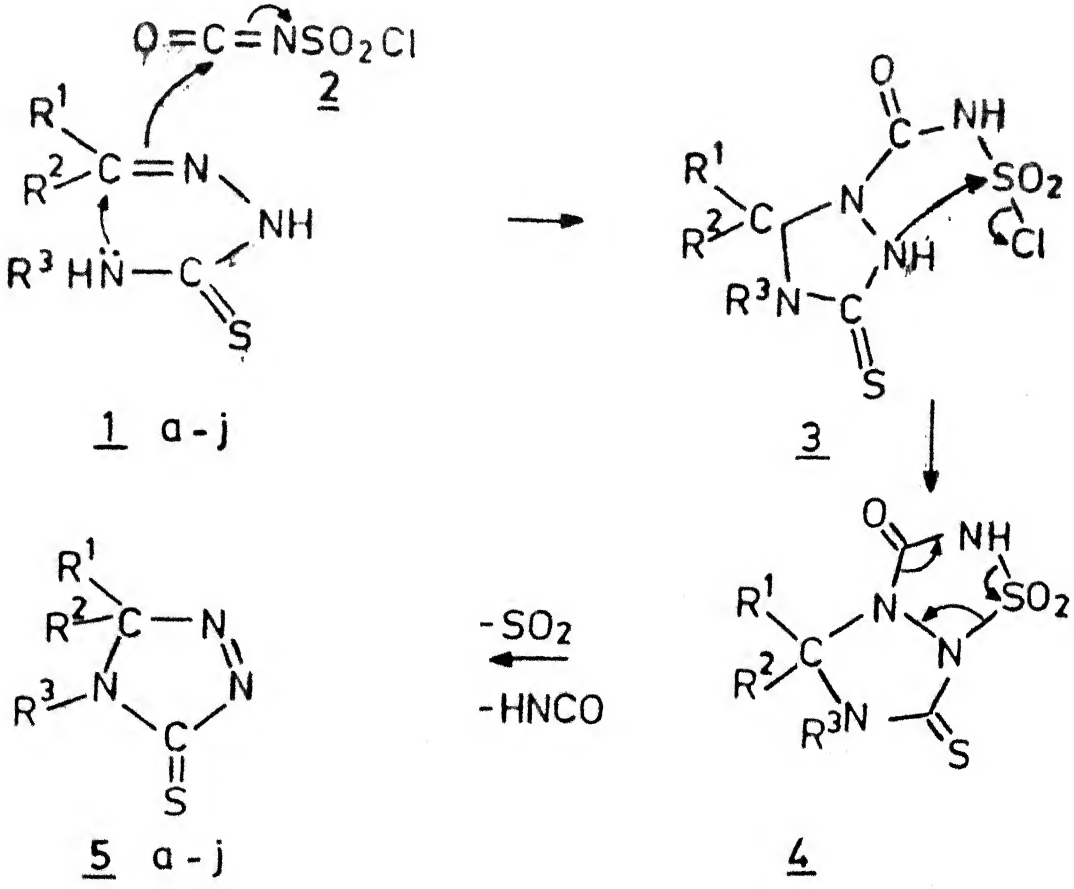
Scheme I.17



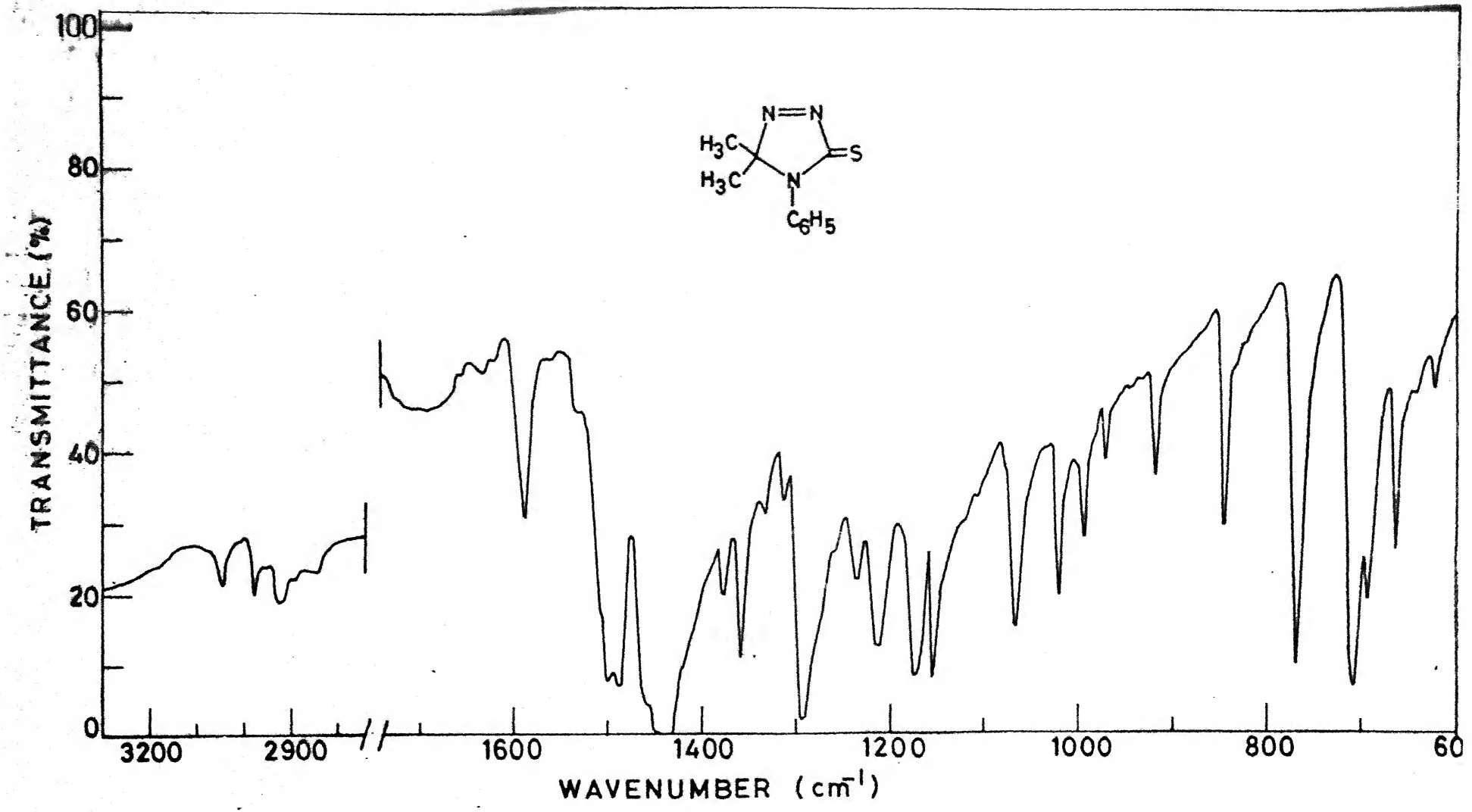
The reaction of CSI with 2-hydroxy aromatic acid chlorides affords a facile method for the synthesis of 2H-1,3-benzoxazine-2,4(3H)-diones[39] (Scheme I.18).

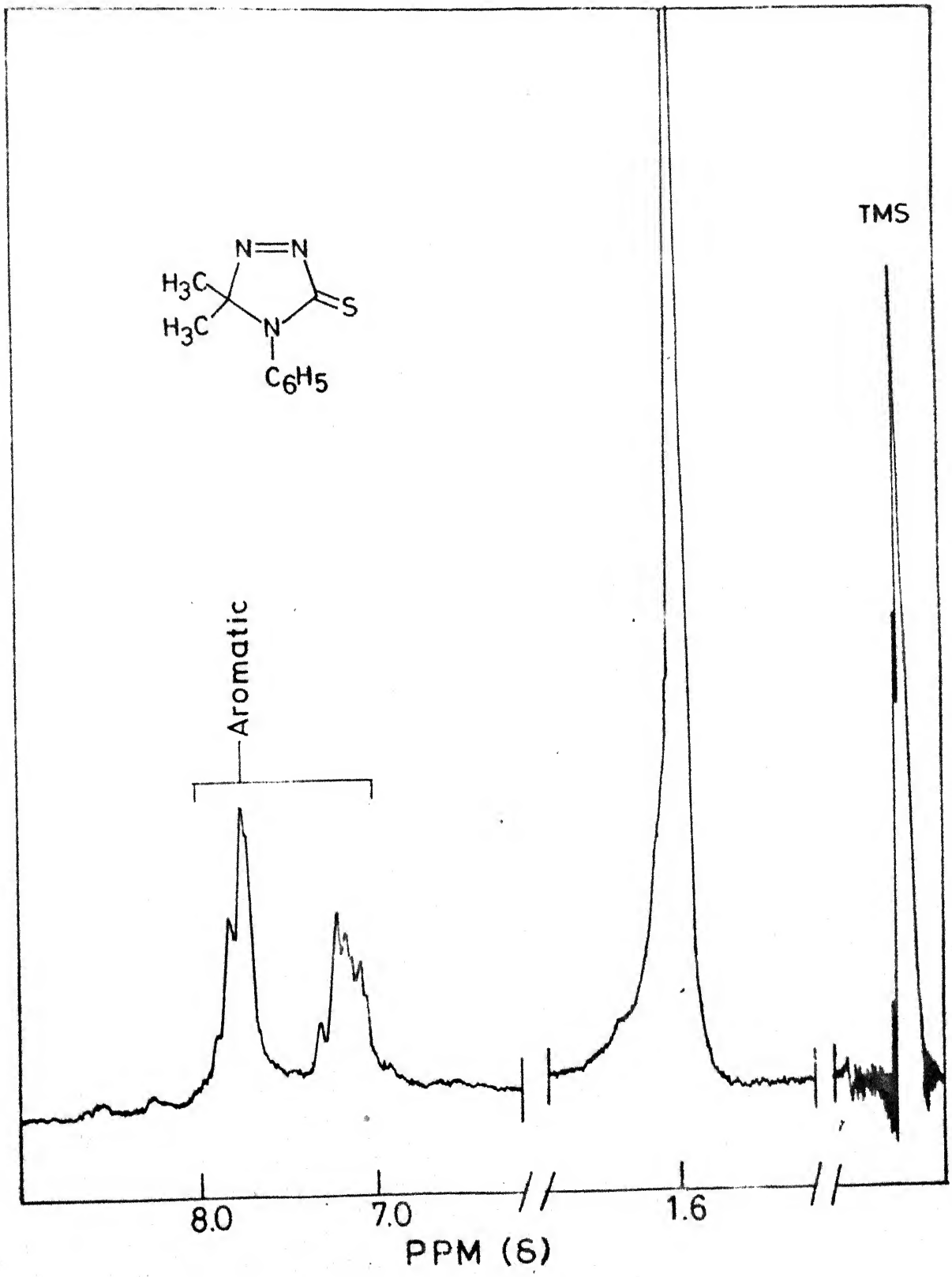
RESULTS AND DISCUSSION

Chlorosulfonyl isocyanate is the most reactive isocyanate and has been found to react readily with various 4 aryl thiosemicarbazones to afford Δ'-[1,2,4] triazoline-5-thiones in excellent yields. This method of preparing the above named heterocycle has distinct advantages over that reported in literature, in terms of milder reaction conditions employed, shorter reaction time, and the purity and yield of the product. The reactions are carried



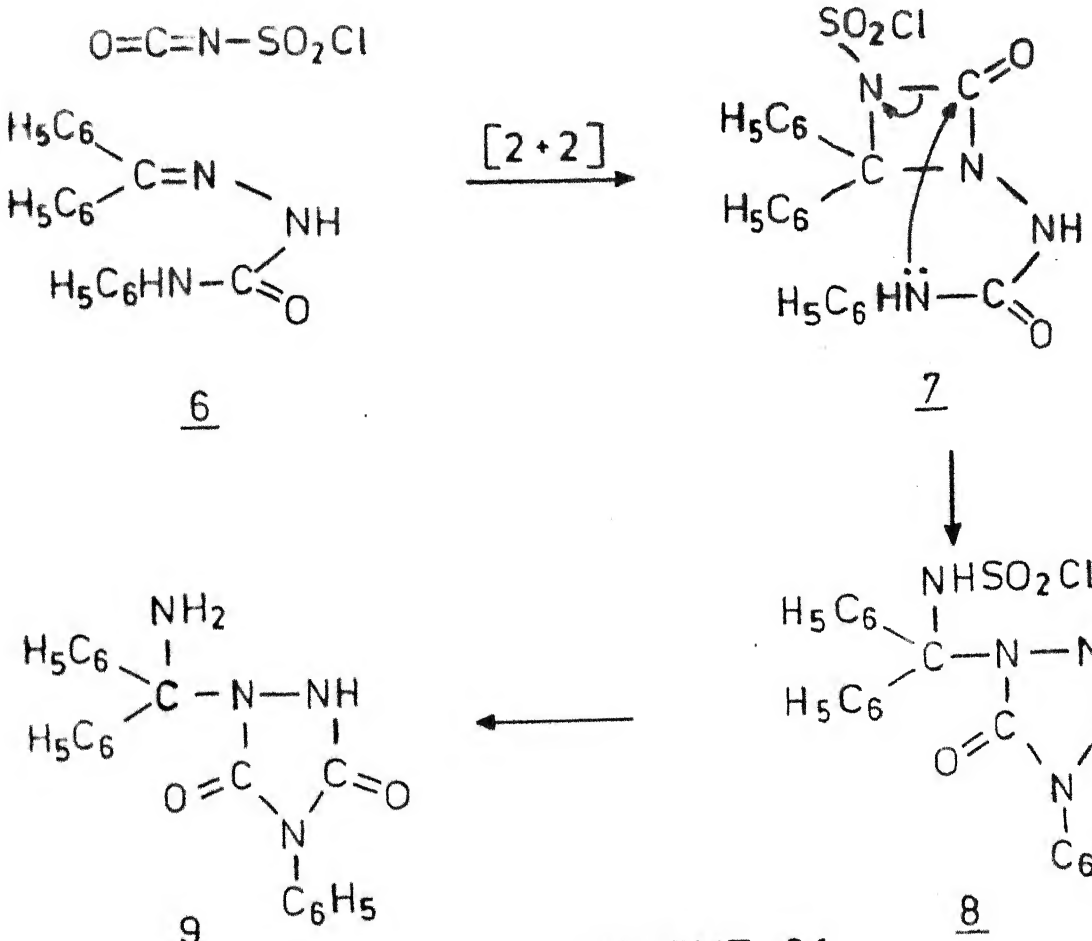
1, 5	R^1	R^2	R^3
a	CH_3	CH_3	C_6H_5
b	CH_3	C_2H_5	C_6H_5
c	$-(CH_2)_5-$		C_6H_5
d	$-(CH_2)_4-$		C_6H_5
e	C_2H_5	C_2H_5	C_6H_5
f	CH_3	CH_3	p-Cl-C_6H_4
g	CH_3	C_2H_5	p-Cl-C_6H_4
h	$-(CH_2)_5-$		p-Cl-C_6H_4
i	$-(CH_2)_4-$		p-Cl-C_6H_4
j	C_2H_5	C_2H_5	p-Cl-C_6H_4


100
80
60
40
20
0
TRANSMITTANCE (%)
3200
2900
1600
1400
1200
1000
800
60
WAVENUMBER (cm⁻¹)
N=N
H3C
H3C
S
N
C6H5


N=N
H3C
H3C
S
N
C6H5
TMS
Aromatic
8.0
7.0
1.6
PPM (δ)

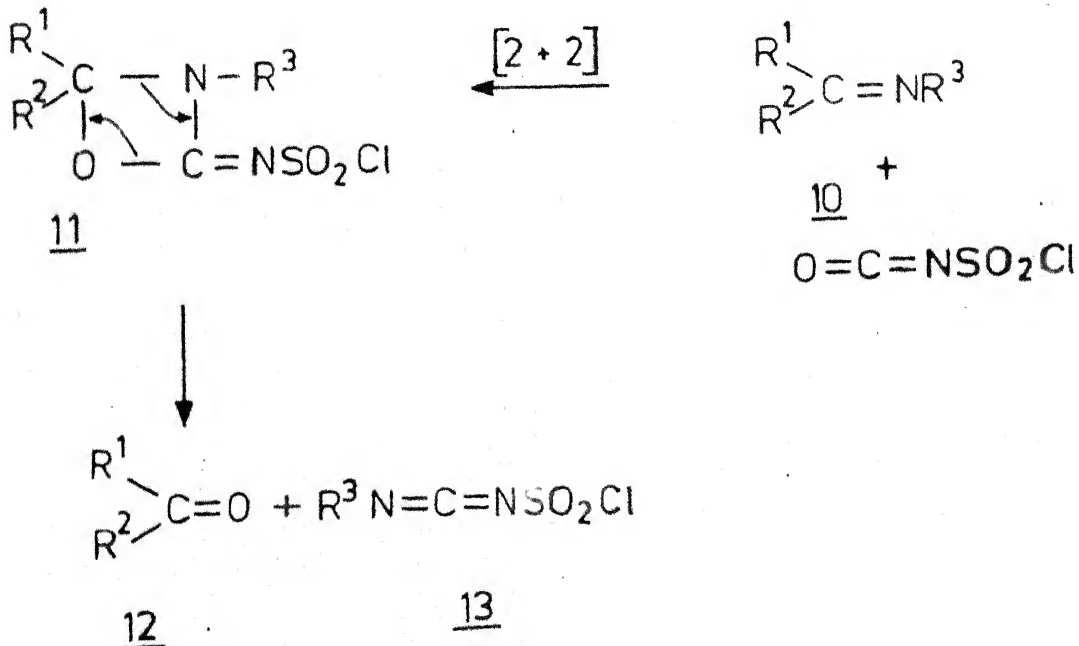
out by adding an equivalent amount of CSI to a stirred solution of 4-aryl thiosemicarbazones in dry dichloromethane at 0^{o}. When the starting material was completely consumed (TLC monitoring), the solvent was removed under vacuum. The resulting material was chromatographed on a silica gel column and eluted with benzene. The pure compounds were isolated by the evaporation of the solvent. The Δ'-[1,2,4]triazoline-5-thiones (obtained in this way) were characterized by comparison with authentic samples, m.p., IR, ^{1}H NMR and mass spectra. A plausible mechanism of various Δ'-[1,2,4]triazoline-5-thiones is depicted in Scheme I.19. Thus, the π-electrons of C=N moiety of 4-aryl thiosemicarbazones attack the strongly electrophilic carbon atom of CSI. The electron deficiency at the carbon of >C=N- is inturn made up by the electron flow from the basic nitrogen atom of the substituted thioamide group. This is, followed by the intramolecular cyclisation leading to the formation of unstable 4. The latter compound loses SO_2 (turns acidified $K_2Cr_2O_7$ paper green). The formation of 4 was detected by infrared spectroscopy of the reaction mixture [1740(ν_{CO}), 1380, 1180 (ν_{SO_2})]cm^{-1}.

Thus, 3,3-dimethyl-4-phenyl Δ'-[1,2,4]triazoline-5-thione (5a), 3 ethyl, 3 methyl-4-phenyl Δ'-[1,2,4]triazoline-5-thione (5b), cyclohexane spiro-3'-(4'-phenyl-Δ'-[1',2',4']triazoline thione) (5c), cyclopentane spiro-3'-(4'-phenyl-Δ'-[1',2',4']-triazoline-5'-thione) (5d), and 3,3-diethyl-4-phenyl-Δ'-[1,2,4]-

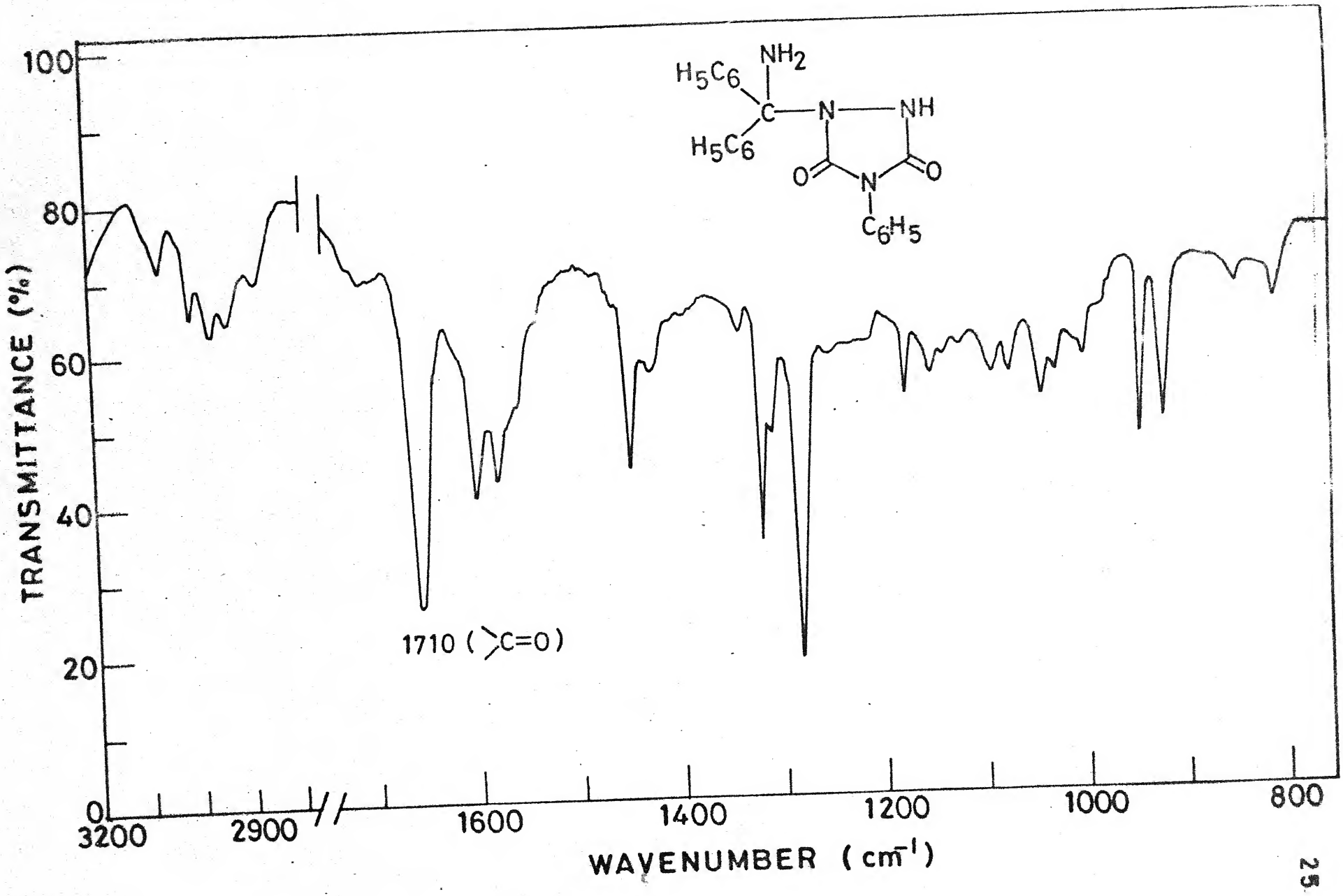


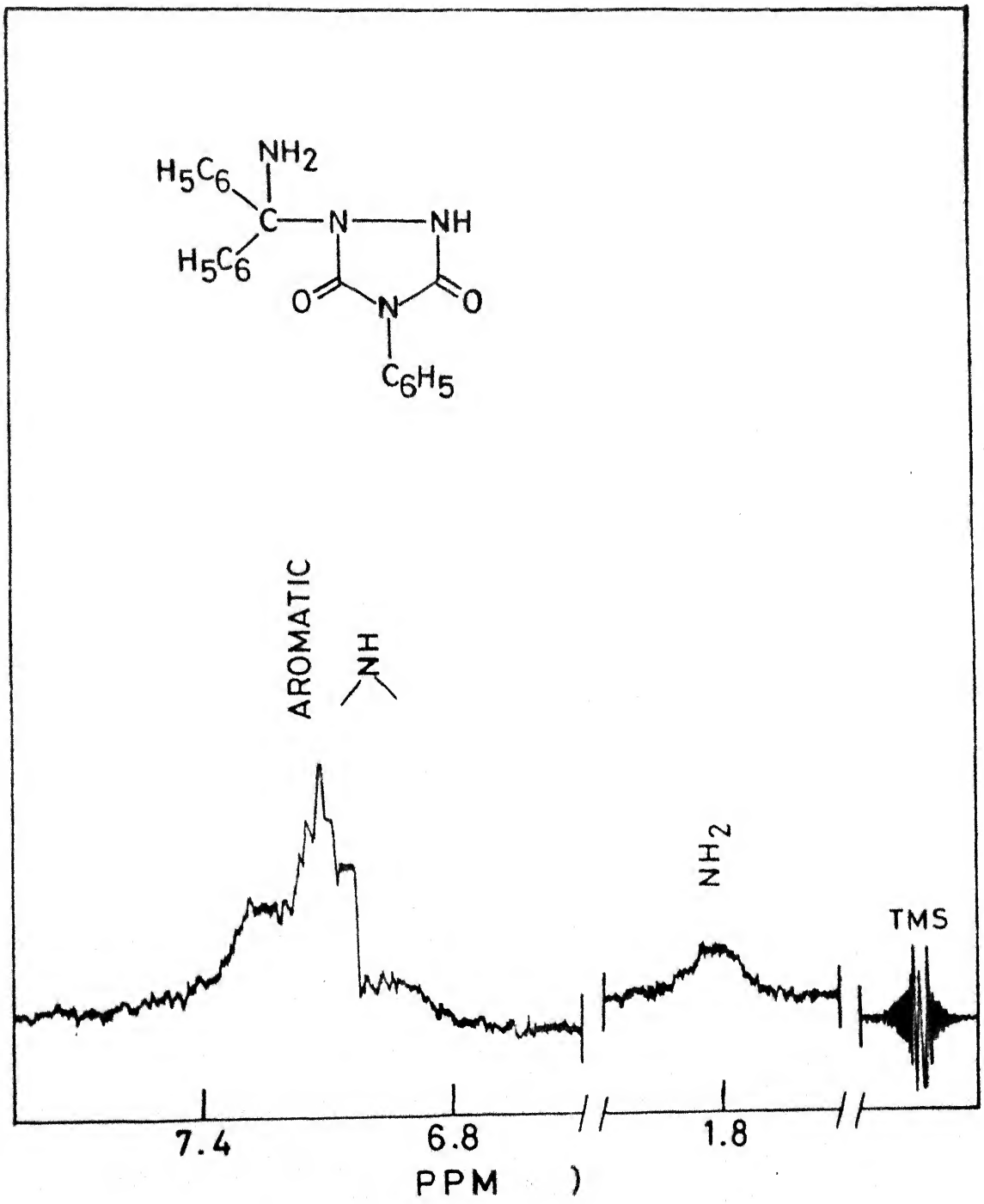
6 7 8 9

SCHEME -21



11 10 12 13


100
80
60
40
20
0
TRANSMITTANCE (%)
3200
2900
1600
1400
1200
1000
800
WAVENUMBER (cm⁻¹)
1710 (>C=O)
H5C6
NH2
C
N
NH
H5C6
O
O
N
C6H5


NH2
H5C6
C
N
NH
H5C6
O
N
O
C6H5
AROMATIC
NH
NH2
TMS
7.4
6.8
1.8
PPM

triazoline-5-thiones (5e) were obtained by the interaction of the appropriate 4-aryl substituted thiosemicarbazones and CSI. The triazoline-thiones corresponding to compounds (5f-k) were prepared similarly by the reaction of 4-p-chlorophenyl/(4-o-bromophenyl)-substituted thiosemicarbazones with CSI.

Reaction of Benzophenone-4-phenyl semicarbazone with CSI in dry dichloromethane at ambient temperature gave 30% yield of benzophenone and 25% of the heterocyclic system (9). The formation of (9) was established from its IR, NMR and mass spectral data. The strong absorption band located at 1710 cm^{-1} indicated the presence of the carbonyl group. The two amino protons appear as a broad singlet at δ1.8 (D_2O exchangeable). The other proton attached to nitrogen appear in the aromatic region in ^1H NMR spectrum. The formation of the products has been rationalized as shown in (Scheme I.20). The reaction of 4-aryl semicarbazones proceeds through [2+2] cycloaddition, with the formation of the intermediate 7. The NH group attacks the electrophilic carbonyl carbon atom to yield (8). The latter compound on hydrolysis affords (9). The ketoschiff's bases with CSI have been found to give the corresponding keto compounds in a quantitative yield. The deprotection of keto schiff's bases is visualised to proceed via a pathway as depicted in (Scheme I.21). Reaction of 2,3-diphenyl-5,6-dihydropyrazine with CSI in dichloromethane afforded benzil in quantitative yield. The compound was further

characterized on the basis of the IR, ^{1}H NMR and mass spectral data and comparison with an authentic sample of benzil.

Experimental:

All the melting points are uncorrected and were taken on Fischer-Johns melting point apparatus. The IR spectra were recorded on Perkin-Elmer model-580 Infra-red spectrophotometer. PMR spectra were recorded on Varian EM-390 (90 MHz) instrument. Chemical shifts are reported in parts per million downfield from the internal reference TMS (δ). Multiplicity is indicated using the following abbreviations (singlet), bs (broad singlet), d (doublet), t (triplet). Mass spectra were recorded on a Jeol JMS-300D mass spectrometer at 70 eV. The elemental analyses were carried out in Coleman automatic carbon, hydrogen and nitrogen analysers.

Starting materials:

Chlorosulfonyl isocyanate was purchased from Fluka AG, Switzerland and was used as such.

Preparation of 4-phenyl thiosemicarbazone:

Phenyl isothiocyanate (6.68g) was dissolved in alcohol (20 ml). To this solution, hydrazine hydrate (2.0g) was added with sufficient cooling at 0^{o}. The titled compound precipitated as

a white solid. It was filtered and recrystallized (ethanol) m.p., 138° (lit.[40] 140°).

Preparation of Acetone-4-phenyl thiosemicarbazone:

The titled compound was prepared by adding a slight excess of acetone to a boiling saturated alcoholic solution of the 4-phenyl thiosemicarbazone. The refluxing was continued for the additional 15 minutes. The thiosemicarbazone separated on cooling in glistening plates and after recrystallizing (EtOH) melted at 129° (lit.[41], 130°).

Preparation of 4-p-chlorophenyl isothiocyanate:

Concentrated ammonia solution (41 ml; d,0.88) was added slowly with stirring to a solution of p-chloroaniline (33.13g, 0.26 mol), carbon disulfide (24 ml) and rectified spirit (40 ml) at 10-15°. The flask was cooled in a freezing mixture (ice-salt) to obtain dithiocarbamate. It was allowed to stand overnight, filtered and was washed with a little ether. This was then dissolved in water (1500 ml) and stirred mechanically while a solution of lead nitrate (87g, 0.26 mol) in water (175 ml) was slowly added. The stirring was continued for 20 minutes and p-chloro-phenyl isothiocyanate was isolated by steam distillation into a receiver which contained sulfuric acid (5 ml, 0.5 M). The

solid product was filtered and was washed with a little water, m.p., 60° (lit.[42] 61°).

Preparation of 4-(p-chlorophenyl)thiosemicarbazone :

4-(p-chlorophenyl)thiosemicarbazone was prepared by mixing hydrazine hydrate and p-chlorophenyl isothiocyanate in ethanol (1:1 mol) with cooling (0°). The product obtained was filtered and recrystallized with ethanol m.p., 191° (lit.[43], 192°).

Preparation of 4-(p-chlorophenyl)thiosemicarbazones of various ketones (General Method)

These compounds were prepared by adding ketone to a boiling saturated alcoholic solution of the 4-(p-chlorophenyl)thiosemicarbazone. The titled compounds were separated on cooling the reaction mixture.

4-o-Bromophenylthiosemicarbazide

o-Bromoaniline (17.2g) and phenyl isothiocyanate (13.5g) in ethanol (50 ml) were heated under reflux for 1.5 h. The product crystallised out on cooling. Recrystallization of the crude product with, ethanol furnished N^1-2-bromophenyl-N^2-phenyl-thiourea.

Hydrazine hydrate (1.2g) in ethanol (75 ml) was added to N^1-2-bromophenyl-N^2-phenyl-thiourea (7.1g). The reaction mixture

was refluxed for 9 h and the solvent distilled off under reduced pressure. The syrupy residue was triturated with light petroleum and then crystallised from ethanol to give 4-o-bromophenylthiosemicarbazide, m.p., 152° (lit.[44], 153°).

Preparation of 4-o-Bromo-phenyl acetone thiosemicarbazone:

The titled compound was prepared by heating the thiosemicarbazide with the acetone in ethanol in the usual manner, m.p. 142° (lit.[41], 144°).

A General Method for the syntheses of 5(a-k)

CSI (0.002 mol) was added at 0-5° to a stirred solution of (1a-k) (0.002 mol) in dry dichloromethane (5 ml). The stirring was continued for 15 minutes and the reaction mixture was allowed to attain room temperature. The stirring was continued for additional 3 h. The solvent was removed under vacuum. The resulting material was chromatographed on a silica gel column and eluted with benzene. Evaporation of the solvent afforded the pure compounds. The yields and melting points are listed in (Table 2).

A General reaction procedure for the formation of ketones from Schiffs bases

CSI (0.08 ml, 0.001 mol), in dichloromethane (4 ml) held at °C, was added dropwise to a stirred solution of Schiffs bases

(0.001 mol) in dichloromethane (6 ml). As soon as the reaction was complete, the reaction mixture was diluted with water, and saturated with sodium chloride and extracted with ethyl acetate (2x10 ml). Removal of the solvent gave the corresponding ketones in quantitative yields. The yields and the products obtained are listed in Table-3.

Reaction of 2,3-diphenyl-5,6-dihydropyrazine with CSI

CSI (0.08 ml, 0.001 mol) in dry dichloromethane (5 ml) was added dropwise at 0° to a stirred solution of 2,3-diphenyl-5,6-dihydropyrazine (0.236g, 0.001 mol) in dry dichloromethane (5 ml). As soon as the reaction was complete (TLC monitoring) the solvent was removed and to the residue aqueous acetone (10:1, 5 ml) was added. The reaction mixture was then extracted with ether (3x10 ml). The ether extract was dried (Na_2SO_4). Removal of the solvent gave a residue. The residue was found to be identical with an authentic sample of benzil and on the basis of IR, NMR and m.p. data. Yield 0.189g (90%), m.p. 94-95°.

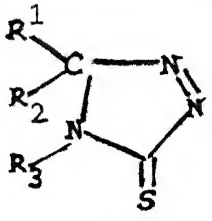
Calcd for $C_{14}H_{10}O_2$: C: 80.00; H: 4.76

Found : C: 80.06; H: 4.83%

IR spectrum (KBr) ν_{max} : 1670 cm^{-1} (ν_{CO}).

TABLE 2

Δ'-[1,2,4]-Triazoline-5-thiones

Compd. No.		Yield (%)	M.pt. (°C)	
			Observed	literature
5a	$R_1=R_2=CH_3$, $R_3=C_6H_5$	95	175	174
5b	$R_1=CH_3$, $R_2=C_2H_5$, $R_3=C_6H_5$	92	125	123
5c	$R_1,R_2=-(CH_2)_5-$, $R_3=C_6H_5$	89	190	188
5d	$R_1,R_2= -(CH_2)_4-$, $R_3=C_6H_5$	87	168	165
5e	$R_1=R_2=C_2H_5$, $R_3=C_6H_5$	85	150	151
5f	$R_1=R_2=CH_3$, $R_3=$p-Cl-C_6H_4	93	137	136
5g	$R_1=CH_3$, $R_2=C_2H_5$, $R_3=$p-ClC_6H_4	91	86	90
5h	$R_1,R_2= -(CH_2)_5-$, $R_3=$p-ClC_6H_4	92	208	205
5i	$R_1,R_2= -(CH_2)_4-$, $R_3=$p-ClC_6H_4	90	170	168

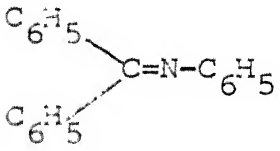
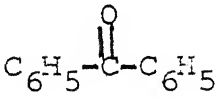
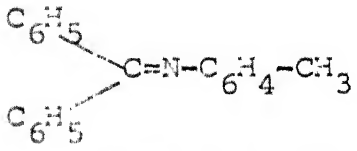
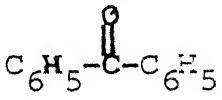
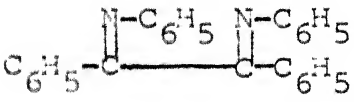
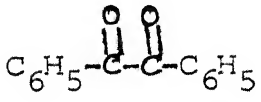
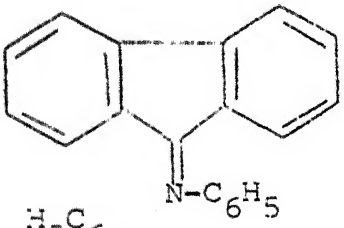
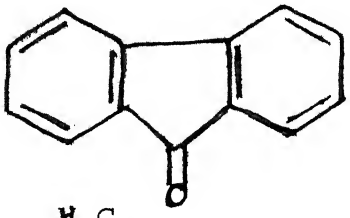
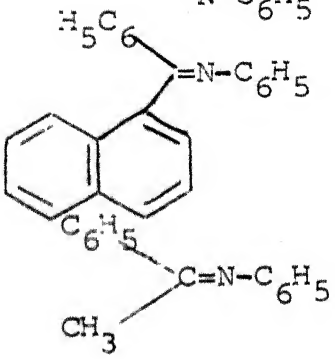
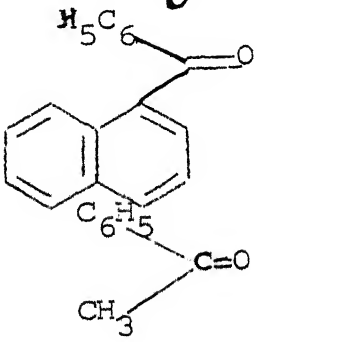
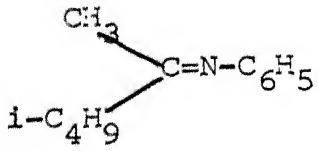
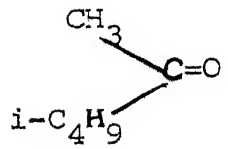
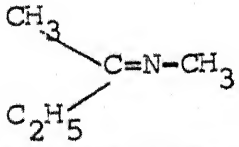
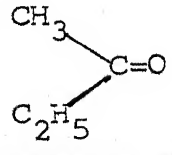
...contd.

TABLE 2(contd.)

5j	$R_1=R_2=C_2H_5$, $R_3=$p-ClC_6H_4	87	125	123
5k	$R_1=R_2=CH_3$, $R_3=$o-BrC_6H_4	88	191	190

TABLE 3

The yields of ketones obtained by the reaction of CSI with keto Schiffs bases.

Reactant	Product	Yield (%)
		82
		78
		80
		77
		79
		81
		84
		83

Synthesis of (5a): Yield: 0.194g (95%), m.p. 175°.

Calcd. Analysis for $C_{10}H_{11}N_3S$: C: 58.53; H: 5.36; N: 20.48

Found : C: 58.74; H: 5.32; N: 20.31%

IR spectrum (KBr) ν_{max}: 3040 (=C-H), 1180($\nu_{C=S}$) cm^{-1}.

PMR spectrum ($CDCl_3$), δ ppm: 1.6 (s, 6H, CH_3), 7.0-8.0 (m, 5H, aromatic).

Mass spectrum : m/z : 205 (M^+).

Synthesis of (5b) : Yield: 0.201g (92%), m.p. 125°.

Calcd. Analysis for $C_{11}H_{13}N_3S$: C: 60.27; H: 5.9; N: 19.17

Found : C: 60.18; H: 5.7; N: 19.23%

IR spectrum (KBr) ν_{max} : 3035 (=C-H), 1170 ($\nu_{C=S}$) cm^{-1}.

PMR spectrum ($CDCl_3$), δ ppm : 1.6 (s, 3H, CH_3), 1.8 (t, 3H, CH_3), 2.4 (q, 2H, CH_2), 6.8-7.5 (m, 5H, aromatic).

Mass spectrum : m/z : 219 (M^+).

Synthesis of (5c) : Yield: 0.218g (89%), m.p. 200°.

Calcd. Analysis for $C_{13}H_{15}N_3S$: C: 63.65; H: 6.10; N: 17.12

Found : C: 63.50; H: 6.27; N: 17.10%

IR spectrum (KBr) ν_{max} : 3045 (=C-H), 1175 ($\nu_{C=S}$) cm^{-1}.

PMR spectrum ($CDCl_3$), δppm: 1.7 (m, 10H, $-CH_2-$), 6.8-7.5 (m, 5H, aromatic).

Mass spectrum : m/z: 245 (M^+).

Synthesis of (5d) : Yield: 0.200g (87%), m.p. 178°.

Calcd. Analysis for $C_{12}H_{13}N_3S$: C: 62.34; H: 5.63; N: 18.20

Found : C: 62.45; H: 5.45; N: 18.32%

IR spectrum (KBr) ν_{max} : 3035 (=C-H), 1180 ($\nu_{C=S}$) cm^{-1}.

PMR spectrum ($CDCl_3$), δppm: 1.6 (m, 8H, $-CH_2-$), 7.0-7.6 (m, 5H, aromatic).

Mass spectrum : m/z: 231 (M^+).

Synthesis of (5e) : Yield: 0.196g (85%), m.p. 150°.

Calcd. Analysis for $C_{12}H_{15}N_3S$: C: 61.80; H: 6.43; N: 18.02

Found : C: 61.72; H: 6.47; N: 18.26%

IR spectrum (KBr) ν_{max} : 3040 (=C-H), 1180 ($\nu_{C=S}$) cm^{-1}.

PMR spectrum ($CDCl_3$) δ ppm : 1.8 (t, 6H, CH_3), 2.3 (q, 4H, CH_2), 7.0-7.6 (m, 5H, aromatic).

Mass spectrum : m/z: 233 (M^+).

Synthesis of (5f) : Yield: 0.222g (93%), m.p. 137°.

Calcd. Analysis for $C_{10}H_{10}ClN_3S$: C: 50.10; H: 4.17; N: 17.53

Found : C: 50.00; H: 4.21; N: 17.90%

IR spectrum (KBr) ν_{max} : 3045 (=C-H), 1170 ($\nu_{C=S}$) cm^{-1}.

PMR spectrum ($CDCl_3$) δ ppm : 1.8 (s, 6H, CH_3), 7.2-7.8 (m, 4H, aromatic).

Mass spectrum : m/z: 239 (M^+).

Synthesis of (5g) : Yield: 0.230g (91%), m.p. 86°.

Calcd. Analysis for $C_{11}H_{12}ClN_3S$: C: 54.23; H: 3.76; N: 15.81

Found : C: 54.41; H: 3.43; N: 15.75%

IR spectrum (KBr) ν_{max} : 3030 (=C-H), 1180 ($\nu_{C=S}$) cm^{-1}.

PMR spectrum ($CDCl_3$), δ ppm : 1.6 (s, 3H, CH_3), 1.8 (t, 3H, CH_3), 2.3 (q, 2H, CH_2), 7.2-8.0 (m, 4H, aromatic).

Mass spectrum : m/z: 253 (M^+).

Synthesis of (5h) : Yield: 0.210g (92%), m.p. 208°.

Calcd. Analysis for $C_{13}H_{14}ClN_3S$: C: 55.81; H: 3.57; N: 15.02

Found : C: 55.65; H: 3.66; N: 14.88%

IR spectrum (KBr) ν_{max} : 3045 (=C-H), 1170 ($\nu_{C=S}$) cm^{-1}.

PMR spectrum ($CDCl_3$), δ ppm : 1.6 (m, 10H, $-CH_2-$), 7.4-8.0 (m, 4H, aromatic).

Mass spectrum : m/z: 230 (M^+).

Synthesis of (5i) : Yield: 0.238g (90%), m.p. 170°.

Calcd Analysis for $C_{12}H_{12}ClN_3S$: C: 54.23; H: 4.51; N: 15.50

Found : C: 54.41; H: 4.39; N: 15.39%

IR spectrum (KBr) ν_{max} : 3040 (=C-H), 1180 ($\nu_{C=S}$) cm^{-1}.

PMR spectrum ($CDCl_3$), δ ppm : 1.7 (m, 8H, $-CH_2-$), 7.2-7.8 (m, 4H, aromatic).

Mass spectrum : m/z: 265 (M^+).

Synthesis of (5j) : Yield: 0.232g (87%), m.p., 125°.

Calcd. Analysis for $C_{12}H_{14}ClN_3S$: C: 53.83; H: 5.23; N: 15.70

Found : C: 53.92; H: 5.31; N: 15.81%

IR spectrum (KBr) ν_{max} : 3045 (=C-H), 1170 ($\nu_{C=S}$) cm^{-1}.

PMR spectrum ($CDCl_3$), δ ppm : 1.8 (t, 6H, CH_3), 2.2 (q, 4H, CH_2), 6.9-7.5 (m, 4H, aromatic).

Mass spectrum : m/z: 267 (M^+).

Synthesis of (5k) : Yield: 0.249g (88%), m.p. 191°.

Calcd. Analysis for $C_{10}H_{10}BrN_3S$: C: 42.25; H: 3.52; N: 14.7!

Found : C: 42.05; H: 3.63; N: 14.81%

IR spectrum (KBr) ν_{max} : 3030 (=C-H), 1170 ($\nu_{C=S}$) cm^{-1}.

PMR spectrum ($CDCl_3$), δ ppm : 1.8 (s, 6H, CH_3), 7.0-7.8 (m, 4H, aromatic).

Mass spectrum : m/z: 284 (M^+).

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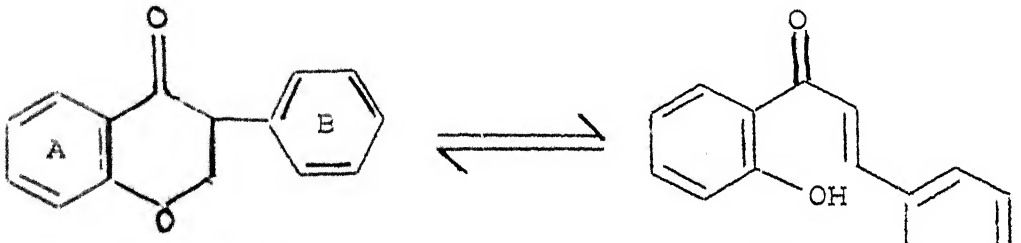
CHAPTER I-B

REACTION OF CSI WITH FLAVANONES

INTRODUCTION

Flavanones are known to occur in plants, either in the free state or as glycosides. Flavanones are 2,3-dihydro-derivatives of the flavones. These are readily interconvertible to the isomeric chalcones.

Scheme I.22

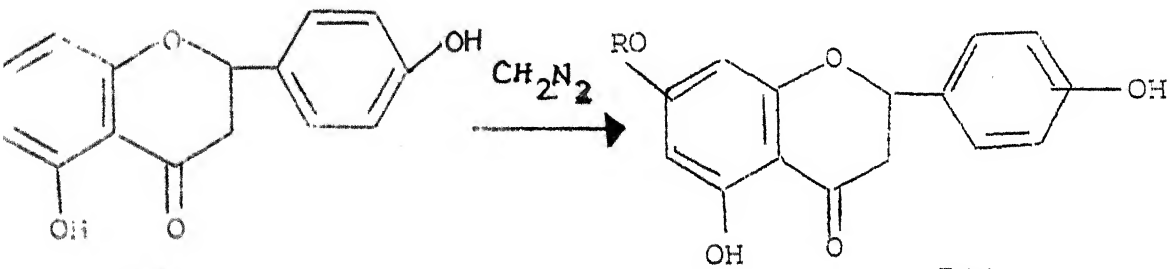


(71) (72)

Flavanones contribute little to the pigmentation, as they are frequently white or cream colored. The most thorough studies of flavanone distribution has been made by Shimokoriyama[1], who followed changes in the flavanones (naringin, poncirin) and flavone (rhoifolin) present throughout a season in the leaves, pistil, filament, petal, bract, flower disc, anther and fruit parts of poncirus trifoliata. In flavanones there is no conjugation between ring B and the carbonyl group, complex interactions

n the molecule are absent. The aromaticity is restricted to the arboxylic ring. In polyhydroxy flavanones the 7-hydroxyl group s the most acidic and 5-hydroxyl group the least reactive. onversely, 7-alkoxyl groups are the least, 5-alkoxyl groups the ost, easily de-alkylated. These tendencies play their part in he conversion[2] of naringenin (73) into sakuranetin (74) by iazomethane.

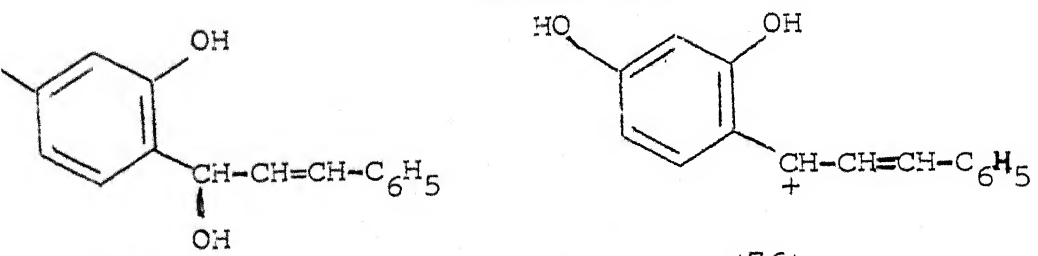
Scheme I.23



(73) (74)

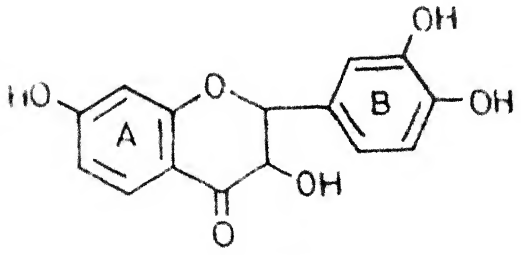
Geissman and Clinton[3] reported that reduction of flavanones nd flavones yield the unsaturated alcohols of type (75). These re well known, to yield highly colored solutions in strong acids ecause of the formation of carbonium ions of type (76).

Scheme I.24

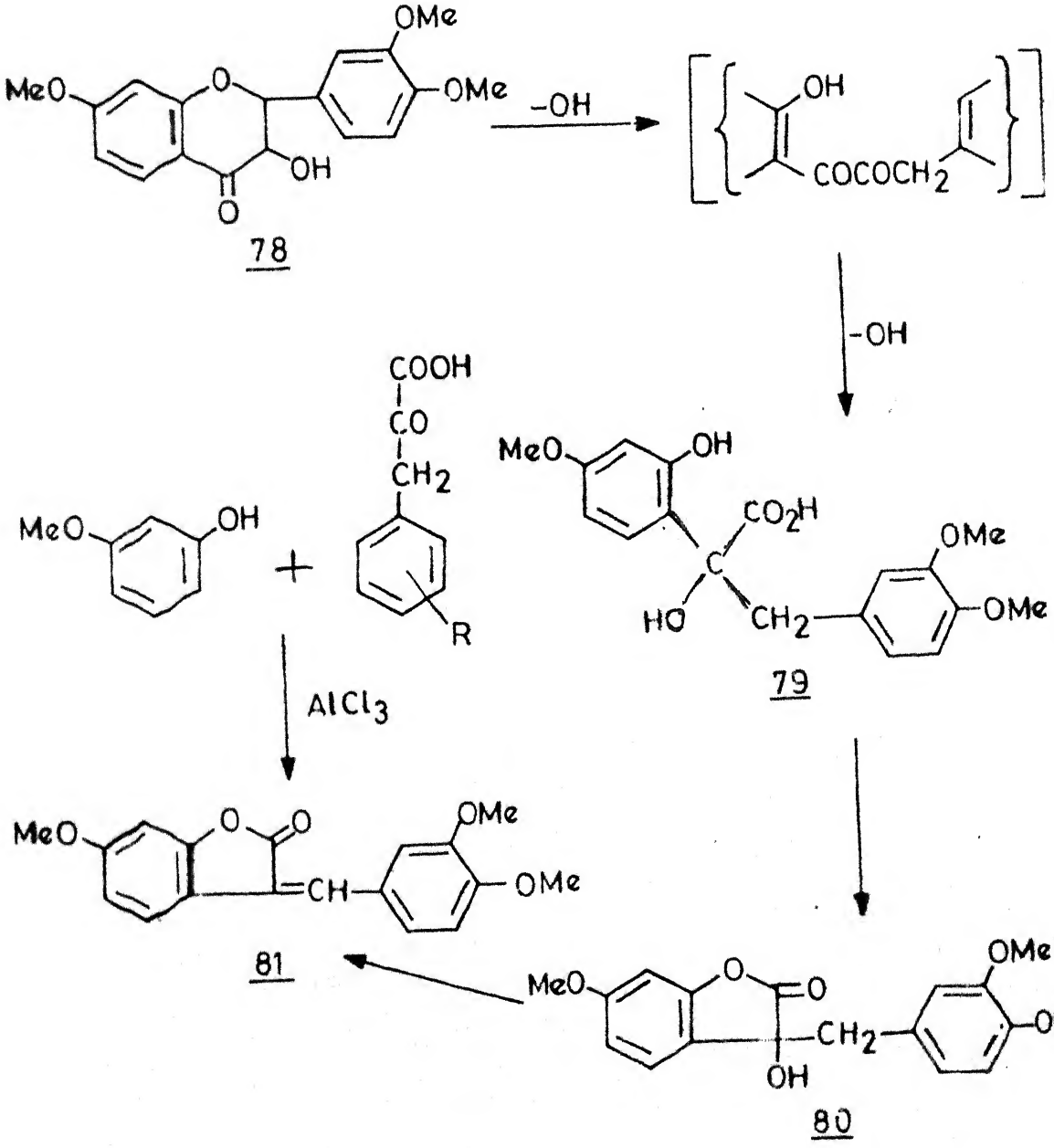


(75) (76)

Scheme 1.25



77



78

79

80

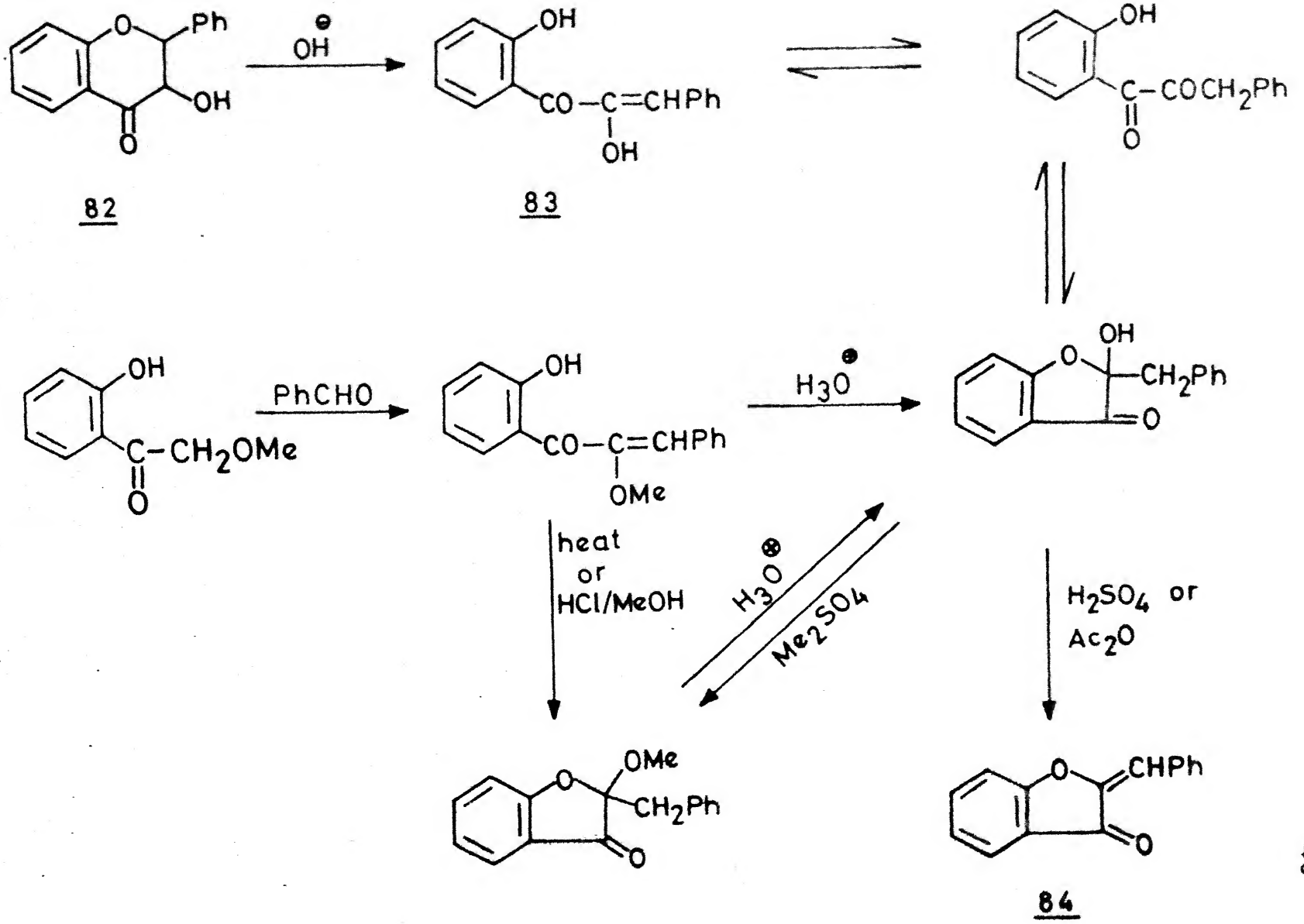
81

The central feature in flavanone chemistry is the reversible ature of the ring opening (71) $\rightleftharpoons$ (72) which affords a chalcone nd is catalysed particularly by bases, as for example, colorless lavanones dissolve in aqueous sodium hydroxide or in sulfuric acid iving bright orange or red solutions. It is known that 6-alkoxy lavanones are unexpectedly resistant[4-5] to ring fission and -substituted flavanones are not easily preparable by cyclizing nalcones[6-8]. The latter effect is thought to be a result of teric hindrance.

The carbonyl group of flavanones undergoes the usual reactions. lconols are produced by lithium aluminium hydride (10) reduction[9], lavans by hydrogenation[10]. Position 3 has the activity usually ssociated with methylenic ketones and is attacked by halogens, -bromosuccinimide and lead tetra-acetate.

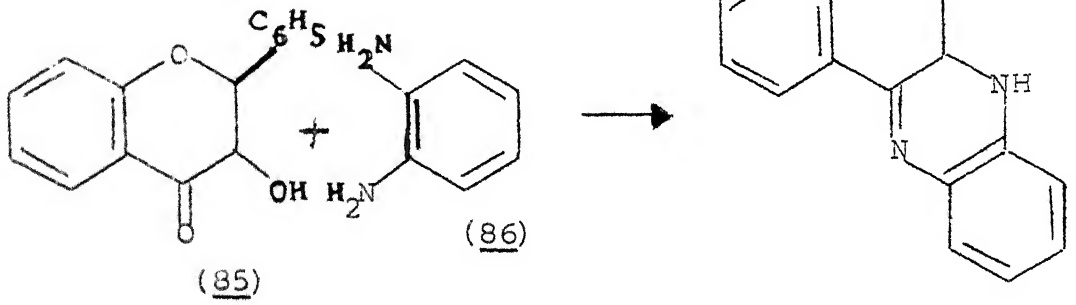
The occurrence of benzilic acid rearrangements was observed y Oyamada[11] during his pioneer studies of fustin (77). The rimethyl ether (78) of this compound gave trimethylhazeic acid 79). It lactonized readily and afforded the annydro-derivatives 80) on being heated with acetic anhydride.

The existence of the ring chain tautomerism, discovered by on Auwers, has long been known and accounts for the facts that -hydroxycoumaranones, though colorless, quickly dissolve in lkali to give red solutions[12]. This is depicted in Scheme I.25.


Ph
OH
O
OH
82
OH
CO–C=CHPh
OH
83
OH
C–COCH2Ph
O
OH
C–CH2OMe
O
PhCHO
OH
CO–C=CHPh
OMe
H3O⊕
OH
O
CH2Ph
O
heat
or
HCl/MeOH
H3O⊕
Me2SO4
H2SO4 or
Ac2O
OMe
O
CH2Ph
O
CHPh
O
84

3-Hydroxy flavanone are said to condense with o-phenylene-diamine to give dihydro quinoxalines[13] as depicted in (Scheme I.26).

Scheme I.26

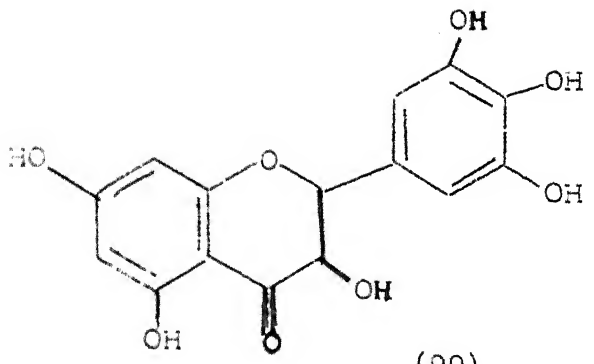


(85) (86) (87)

An unusual loss of a 2-phenyl ring of a flavanone occurs when the compound is treated with thallium trifluoroacetate in trifluoroacetic acid, and the reaction of this kind may occur in nature[14]. Hydroxylated flavanones are sometimes found together with the corresponding chromones.

Flavanones and o-hydroxy chalcones are oxidized by alkaline hydrogen peroxide to 3 hydroxy flavones[15] (flavonols), the reaction proceeding as shown in (Scheme I.26). The final stage may also be accomplished by catalytic hydrogenation. Isonitroso derivative of flavanones also yield flavonols[16] via depicted in (Scheme I.26).

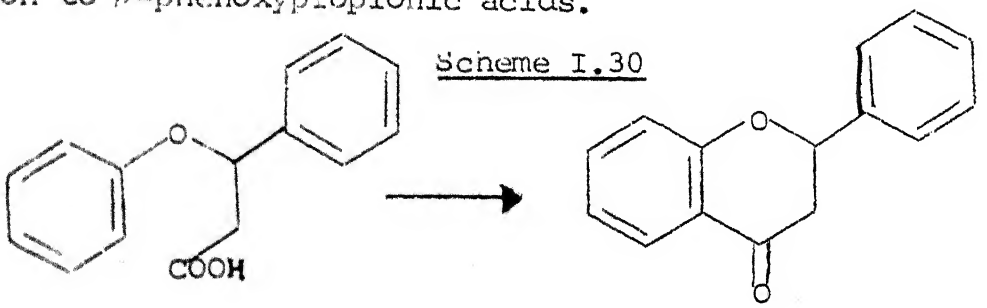
Several flavanones are known to occur in nature. Ampelopsin (99) is an example of a naturally occurring flavanone.



(99)

These can be synthesized by an internal Friedel-crafts reaction to β-phenoxypropionic acids.

Scheme I.30

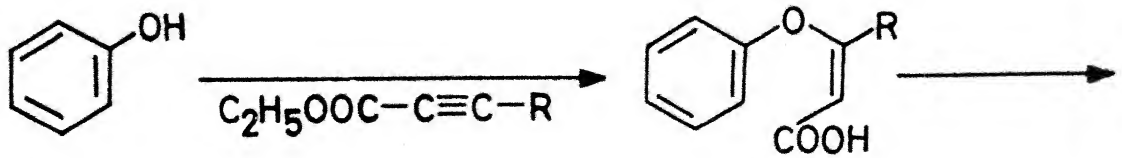


(100) (101)

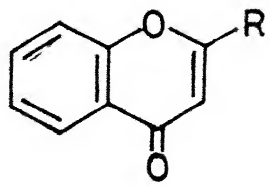
Addition of the sodium salts of phenols to esters of acetylene dicarboxylic acids affords substituted β-phenoxy acrylic acids as shown in (Scheme I.28). It may be cyclized to chromones flavones directly with acetyl chloride or concentrated sulfuric acid, or indirectly through the acid chloride by an internal Friedel-crafts reactions.[17,18]

Wessely-Moser rearrangements are commonly present in flavanone series.[19,20] Flavanones which bear a methoxyl or hydroxyl group ortho to the carbonyl group undergo Wesseley-Mose

Scheme 1.31

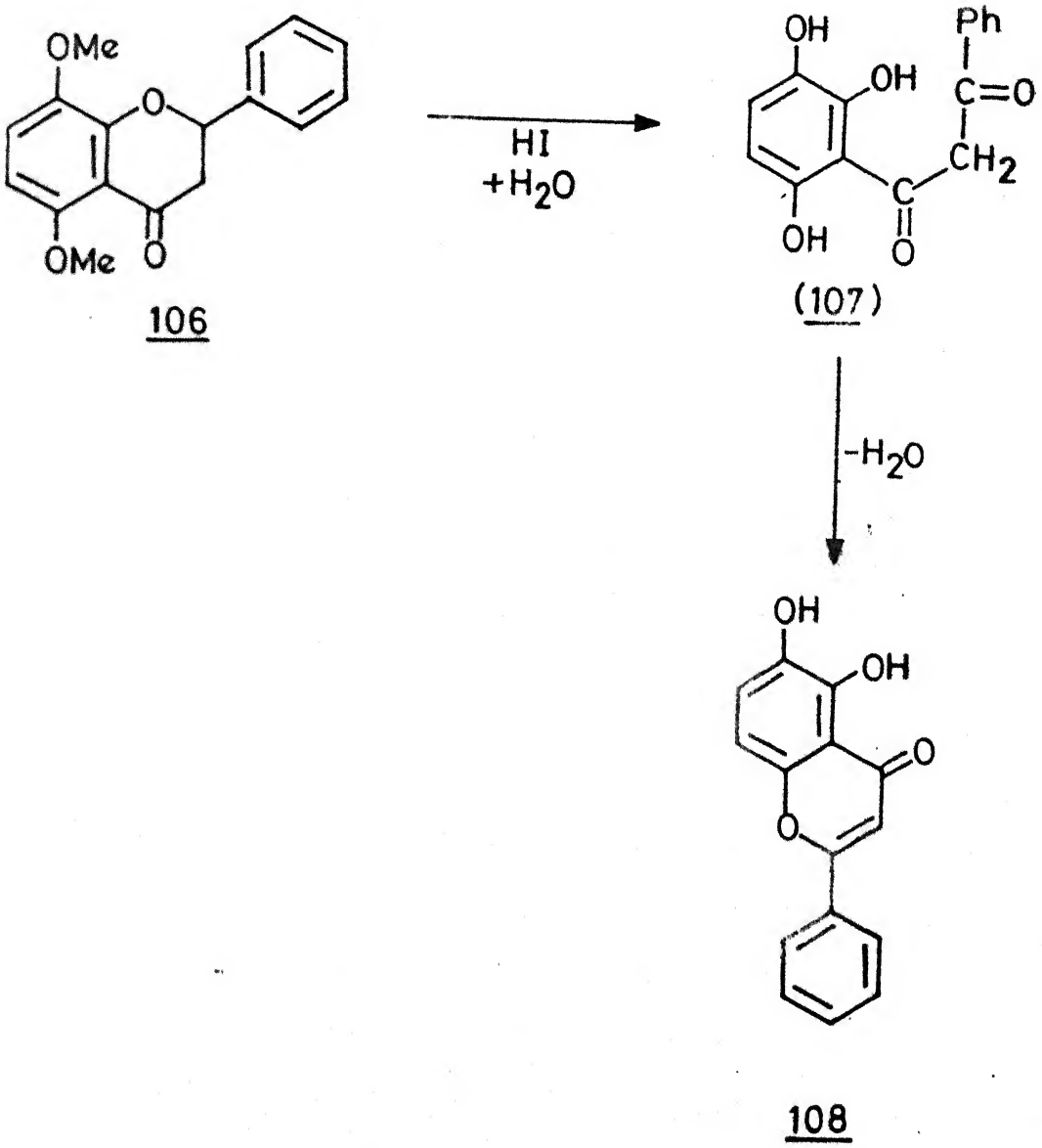


102 103 104



105

Scheme 1.32



106 (107) 108

rearrangement. On heating with hydriodic acid flavanones are demethylated and afford rearranged structure as a result of opening of the flavanone ring and reclosure of the same with a hydroxyl different from that generated during the opening of the ring.

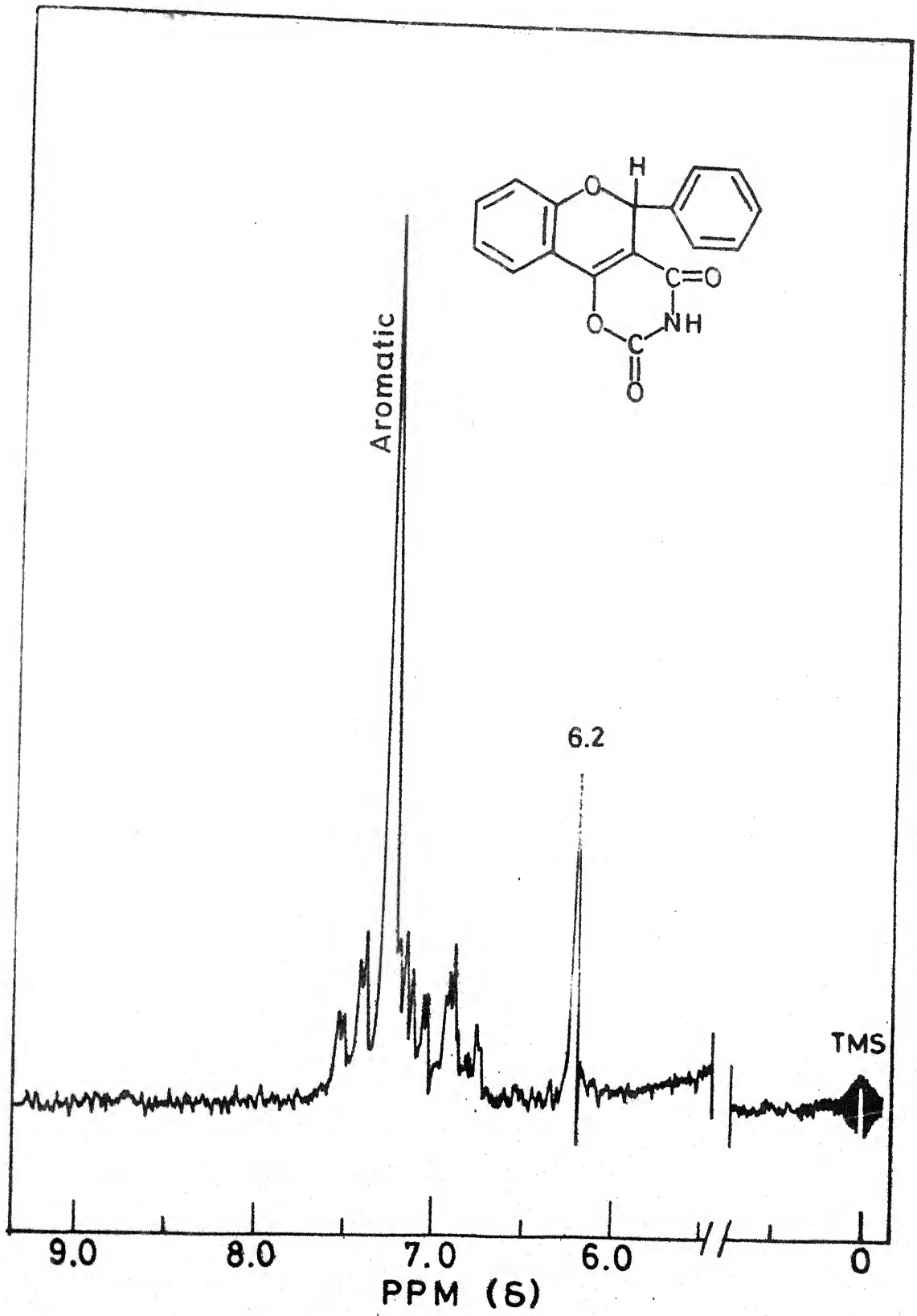
RESULTS AND DISCUSSION

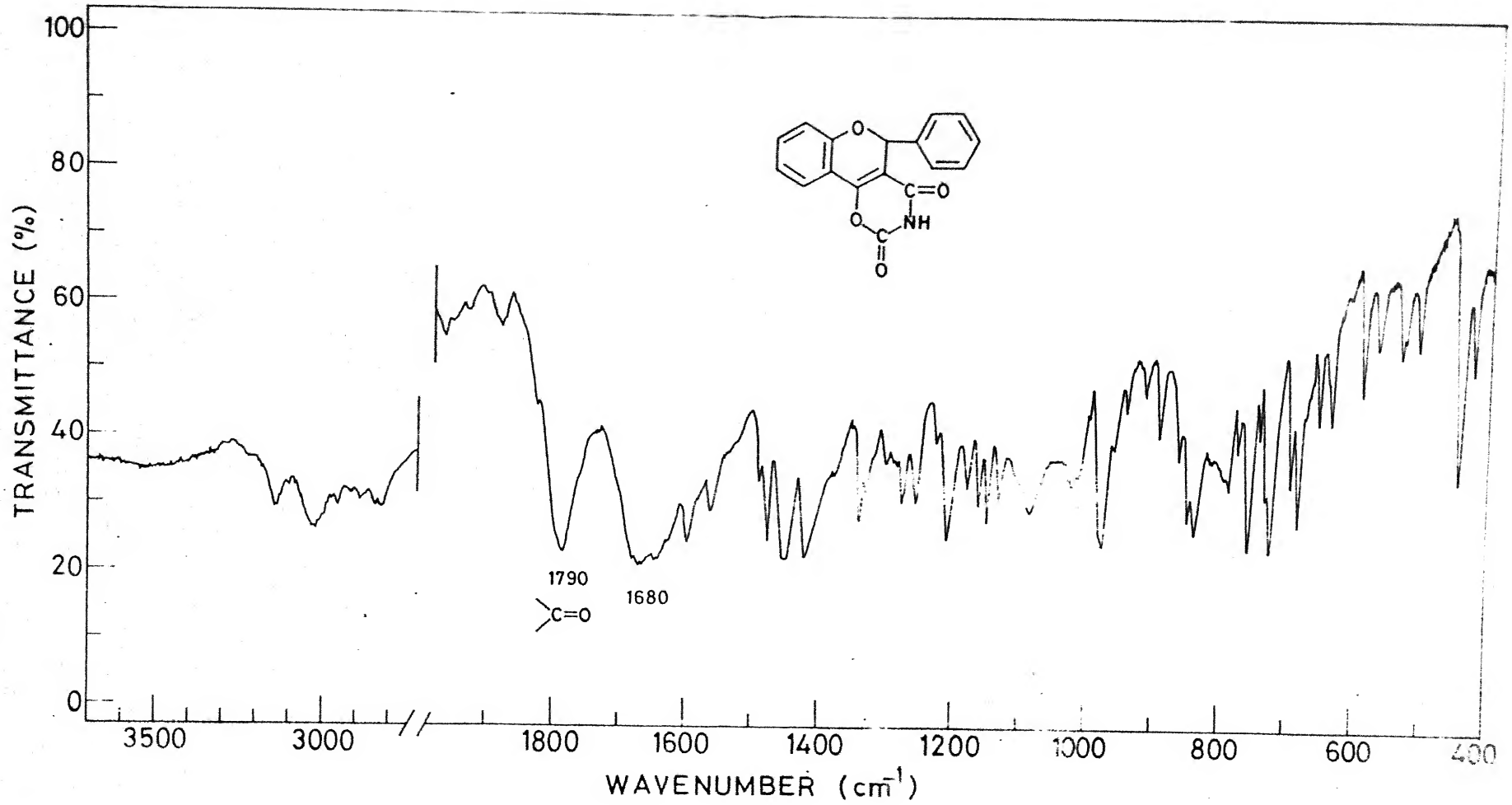
Chlorosulfonyl isocyanate is the most reactive isocyanate and has been found to react with various compounds. With a view to enlarge our understanding about the addition reaction of CSI, we became interested to explore its reactivity towards various compounds, containing active methylene groups. In this context, we selected various flavanones as the suitable substrates. Position-3 in flavanone is susceptible to attack by various reagents. The reactions are carried out by adding an equivalent amount of CSI to a stirred solution of flavanones in dry dichloromethane and the reaction mixture was refluxed for 24 hours. When the starting material was completely consumed (TLC monitoring), petroleum ether was added to the reaction mixture. The red precipitate obtained was acidified with sulfuric acid water (1:3) and was extracted with ether. The distillation of the ethereal layer (after drying it over anhydrous Na_2SO_4) gave yellow residue. It was finally recrystallised from benzene-hexane (1:1) to give the heterocyclic products [109-112]. The products were characterised on the basis of their IR, mass and NMR spectral data. The

IR spectrum showed strong peaks(ν1790 and ν1680 cm^{-1}) of carbonyl groups. The aromatic protons show up as a multiplet at δ 6.8-7.7. The one benzylic proton come up at δ6.2. The NH group is flanked by the two adjacent carbonyl groups, these groups cause deshielding of NH proton and hence appear at off-field. The mass spectral data of the products confirm the assigned structures. The fragmentation pattern observed in the case of(109) exhibits molecular ion peak at m/z 293 and the fragmentation peaks at m/z 265 (M^+-CO), 216 (M^+-C_6H_5), 250 (M^+-HNCO) respectively. The formation of the products is explained as shown by the proposed mechanism (Table 1).

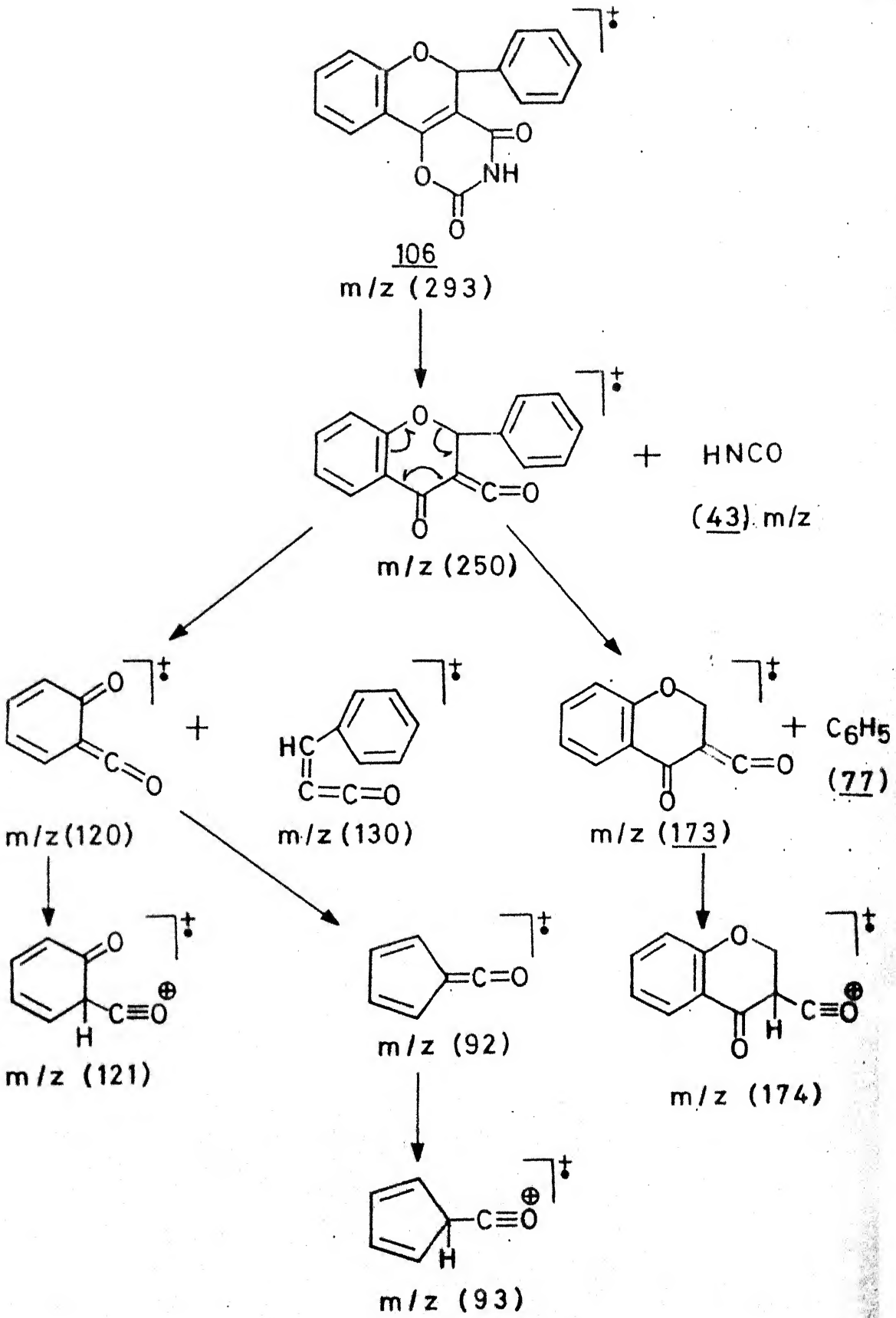
From the mother-liquor the solvent was removed and to the syrupy residue Na_2SO_3 was added, treated with aqueous acetone and the solution was neutralised (pH = 7.5) by the addition of 5% sodium hydroxide solution. The reaction mixture was extracted with ether and was dried over anhydrous Na_2SO_4. The evaporation of the solvent gave the products (113-116).

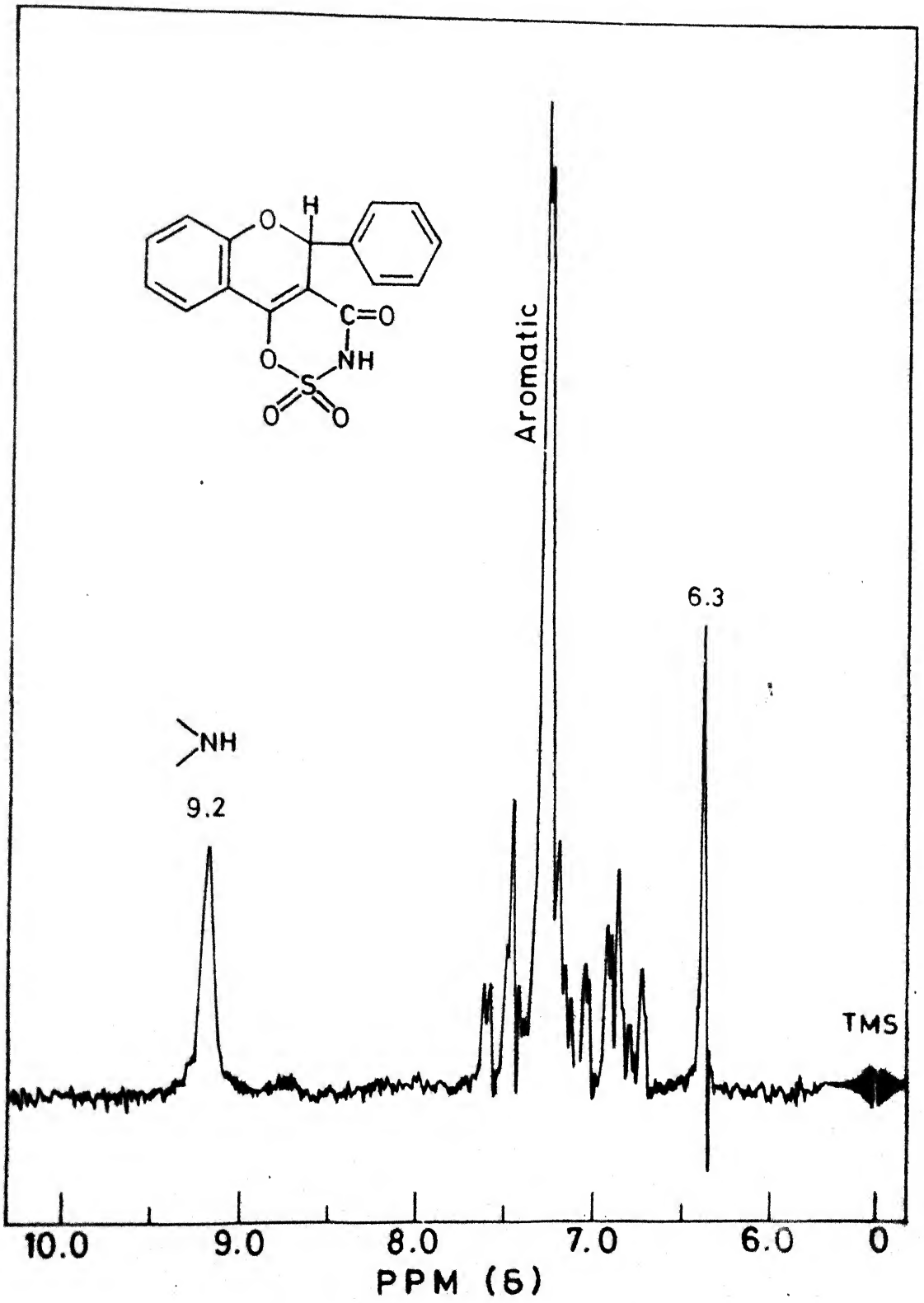
The structures for the above titled compound were arrived at, on the basis of their IR, mass and NMR spectral data. The presence of strong signal at ν 1680 cm^{-1} points to the presence of C=O group. The presence of signals at ν 1380 and ν1170 cm^{-1} indicates the presence of SO_2 group in the molecule. The aromatic protons appear as a multiplet at δ 6.8-7.8 in the N.M.R. spectrum. The NH group (flanked by C=O and SO_2 groups) shows up at lower field (δ 9.2). The benzylic proton exhibits signal at δ 6.3.

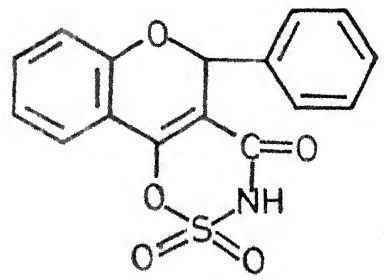

H
O
C=O
NH
O
C
O
Aromatic
6.2
TMS
9.0
8.0
7.0
6.0
0
PPM (δ)

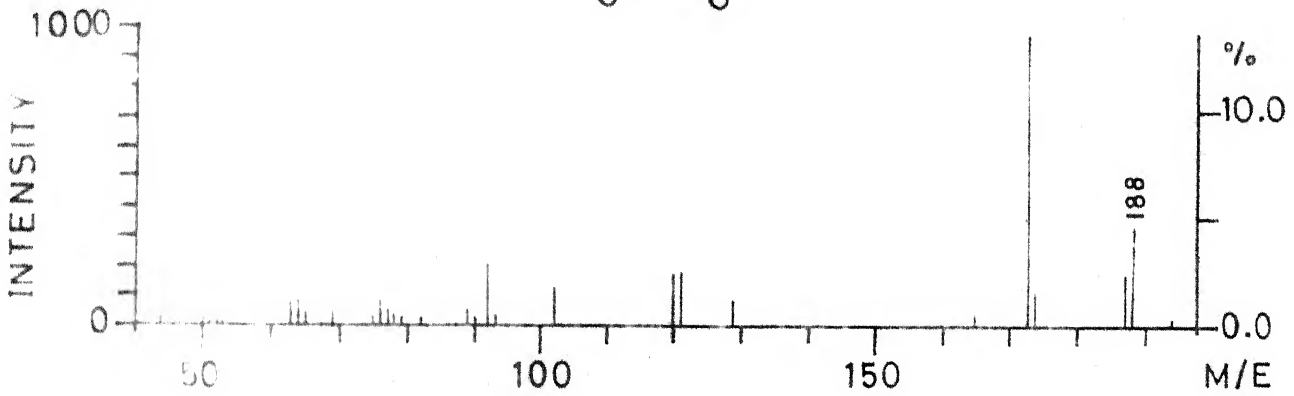

100
80
60
40
20
0
TRANSMITTANCE (%)
3500
3000
1800
1600
1400
1200
1000
800
600
400
WAVENUMBER (cm⁻¹)
1790
C=O
1680
O
C=O
NH
O
C
O

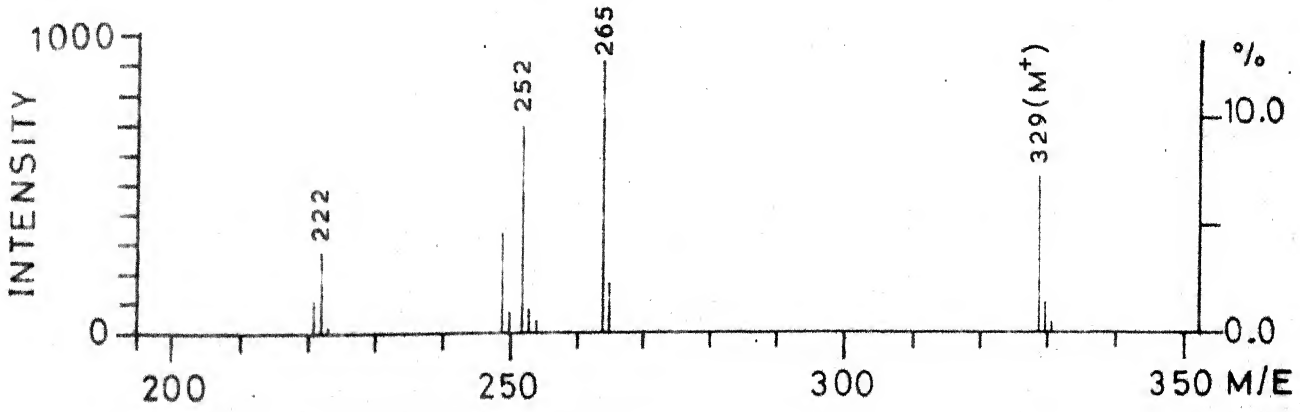
Scheme 1.33

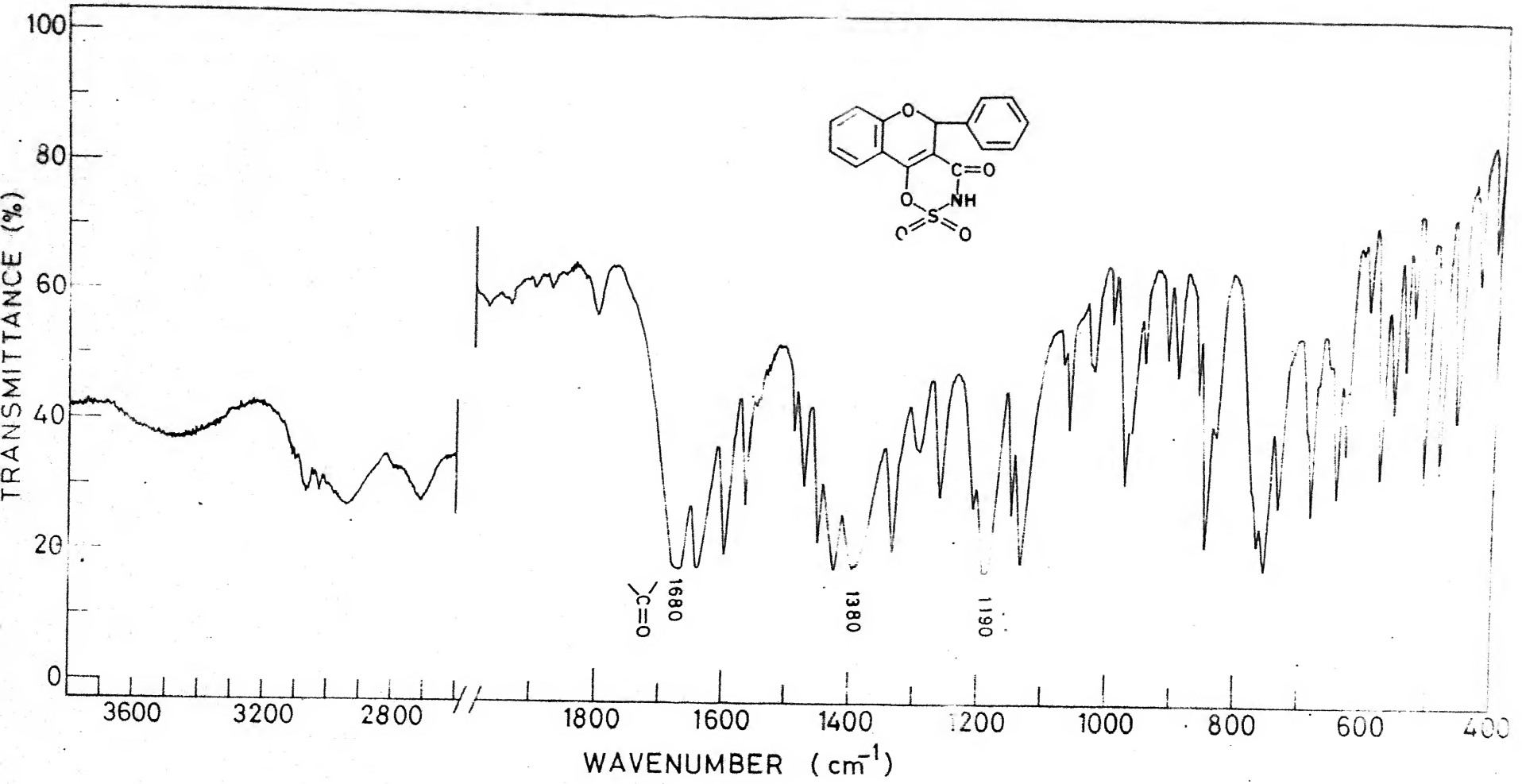

106
m/z (293)
+ HNCO
(43) m/z
m/z (250)
m/z (120)
m/z (130)
+ C6H5
(77)
m/z (173)
m/z (121)
m/z (92)
m/z (174)
m/z (93)


H
O
C=O
NH
O
S
O
O
Aromatic
6.3
NH
9.2
TMS
10.0
9.0
8.0
7.0
6.0
0
PPM (δ)

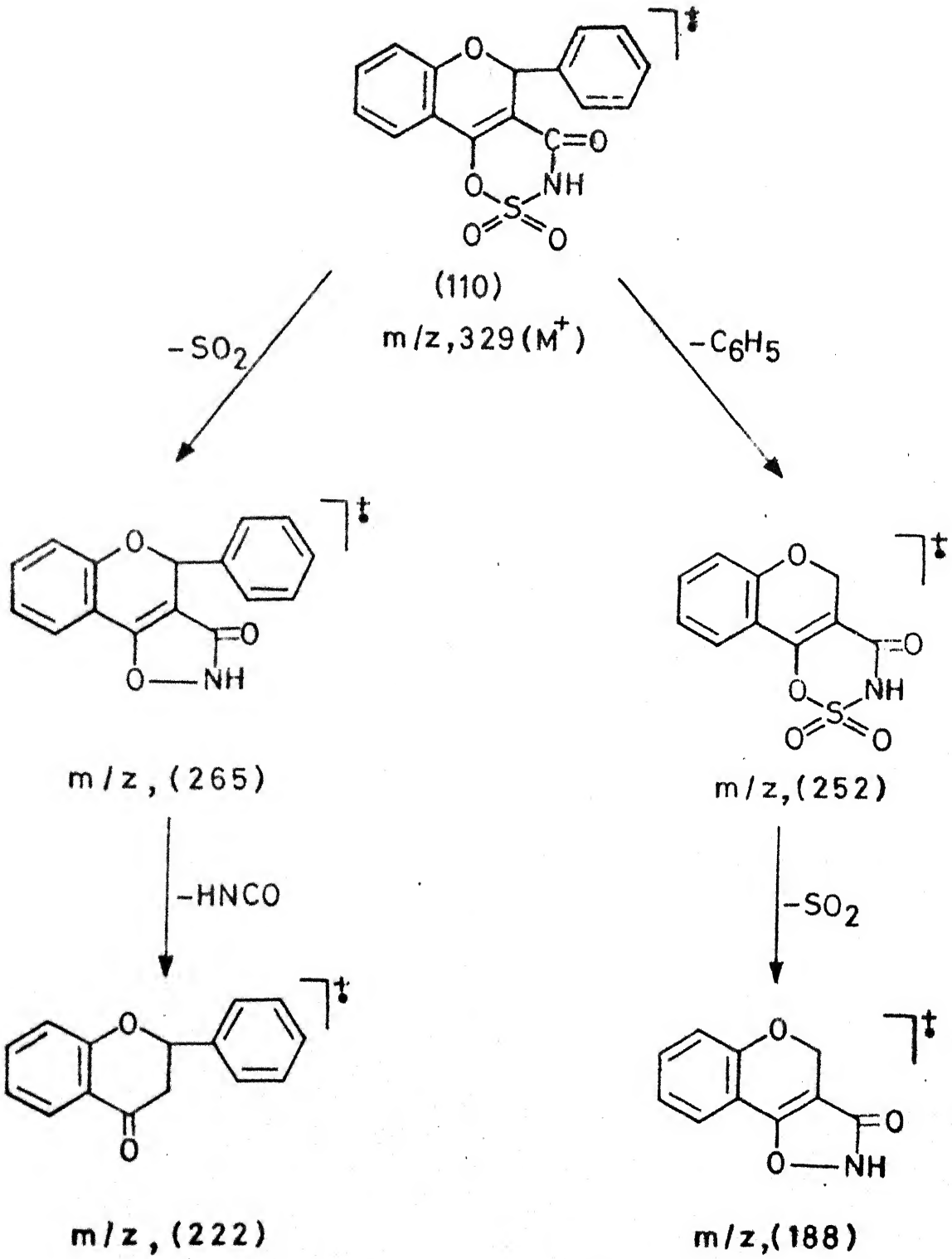

O
C=O
O
NH
S
O
O


1000
INTENSITY
0
%
10.0
0.0
188
50
100
150
M/E


1000
INTENSITY
0
222
252
265
329(M+)
%
10.0
0.0
200
250
300
350 M/E


100
80
60
40
20
0
TRANSMITTANCE (%)
3600
3200
2800
1800
1600
1400
1200
1000
800
600
400
WAVENUMBER (cm⁻¹)
C=O
1680
1380
1190
O
C=O
NH
O
S
O
O

Scheme 1.34



The assigned structure is supported by its mass spectral analysis. The fragmentation pattern observed in the case of (113) is depicted in (Scheme I.34). The spectrum exhibits molecular ion peak at m/z 329 and the fragmentation peaks at 265 (M^+-SO_2), 252 ($M^+-C_6H_5$).

EXPERIMENTAL

Preparation of flavanone

It was prepared in accordance with the procedure described in the literature.[21]

To an alcoholic solution of benzaldehyde (3g) and o-hydroxy acetophenone (3.6g) was added, with continuous stirring, an aqueous solution of NaOH (0.1N, 540 ml). In short time, the reaction became vigorous and the solution turned yellow (pH 9.8). The pasty yellow residue was kept at 37° for 2 days. During this time, it turned into yellow colored oil from which the flavanone was precipitated with water. This was filtered and recrystallized several times with ethanol. Yield, 1.9g, m.p. 73° (lit.[21], 76°).

Preparation of 3',4'-dimethoxy flavanone

2'-Hydroxy-3',4'-Dimethoxy chalcone (5g) was added to hydrochloric acid (120 ml). The resulting solution was refluxed for 8 hrs till the yellow colored solution turned into red liquid. 3',4'-dimethoxy flavanone was obtained by adding water into the mother liquor. The product was recrystallized from ethanol, m.p., 122° (lit.[22], 123-125°).

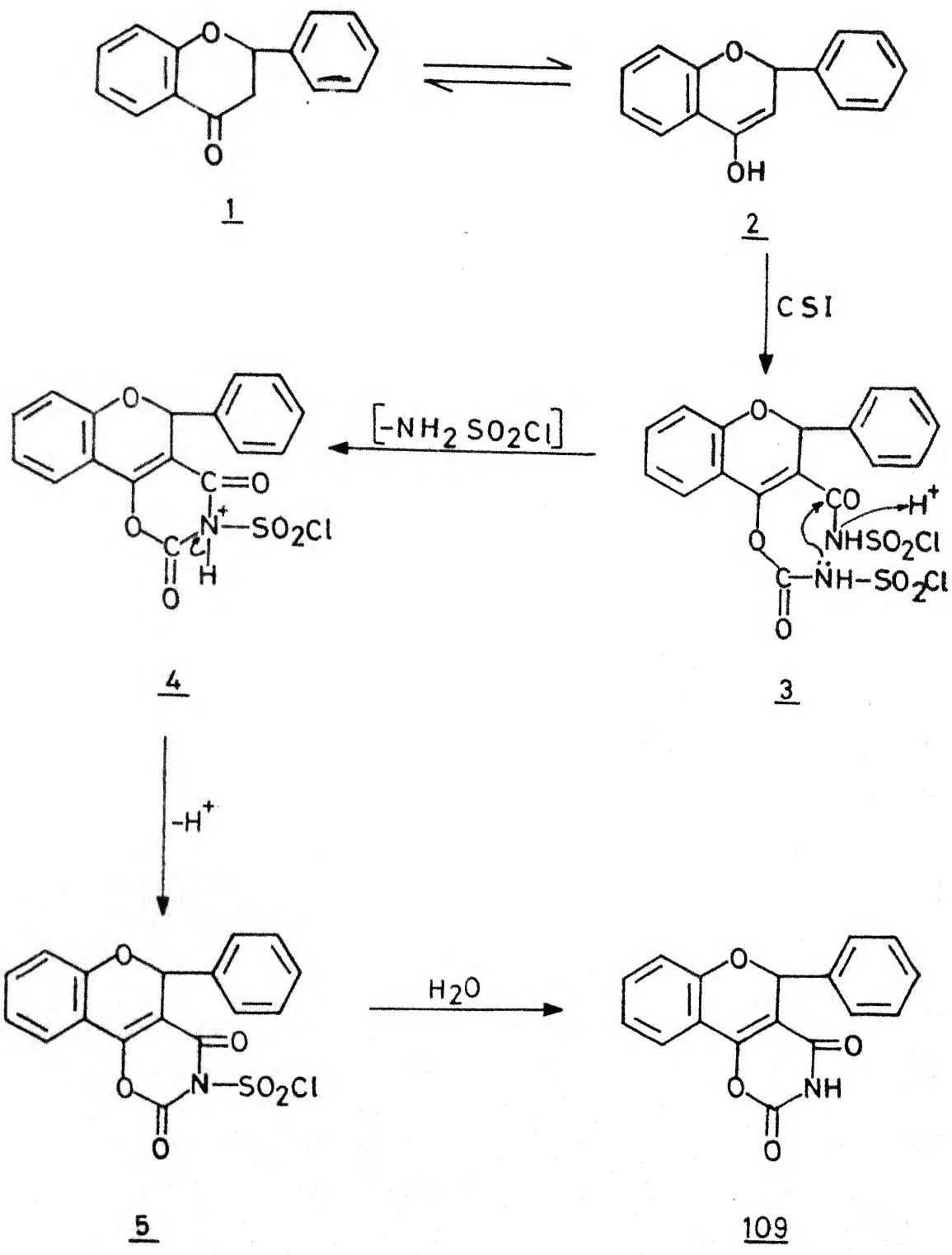
Reaction of flavanones with CSI

All the flavanones that were taken up for our investigation were reacted with CSI according to the following general procedure The m.p. and yields of the products in each case are reported in Table 1.

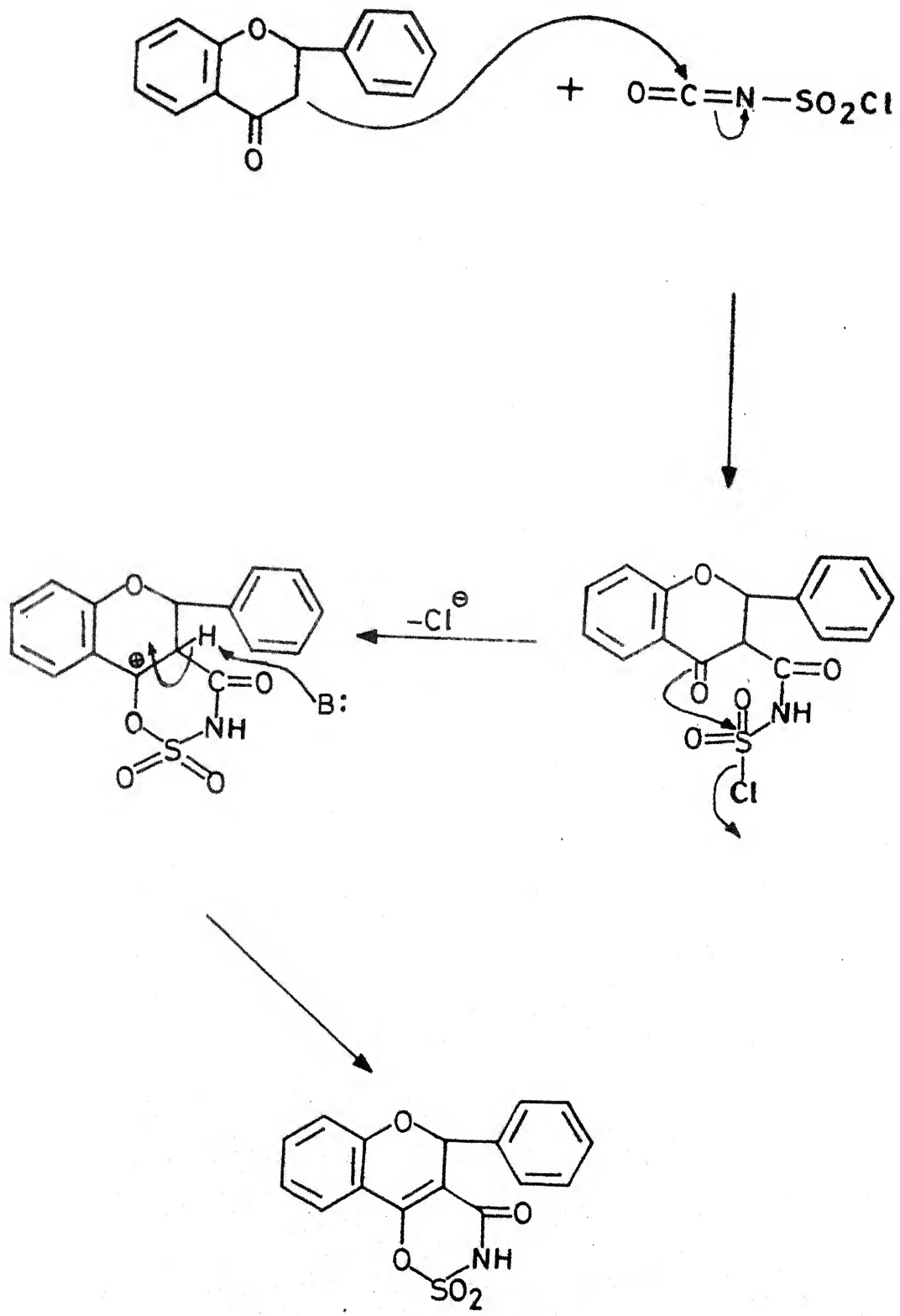
CSI (0.8 ml, 0.01 mol) was added dropwise at room temperature to a solution of flavanone (0.01 mol) in dry dichloromethane (15 ml). The reaction mixture was refluxed for 24 hours with continuous stirring. After the completion of the reaction petroleum ether was added to the resulting solution. The red precipitate thus obtained, was dissolved in acetone-water, acidified with sulfuric acid water (1:3), and extracted with ether. The evaporation of the solvent (after drying it over anhydrous sodium sulfate) gave a yellow pasty mass. It was then crystallized from benzene-hexane to give light yellow colored needles.

From the mother liquor, solvent was removed. To the residue obtained sodium sulphite was added, it was then treated with aqueous-acetone (5 ml, 10:1) and allowed to stand for 1h. The solution was neutralised (pH = 7.5) by careful addition of 5% sodium hydroxide solution and was extracted with ether. The ether extract was dried (Na_2SO_4). Removal of the solvent gave the product as white needles.

Scheme 1.35



Scheme I.36



113

The plausible mechanism involved in the formation of (113) by the reaction of flavanone with CSI is depicted in (Scheme I.36). The reaction occurs under the catalytic influence of a base.

The formation of (109) is postulated to involve a different pathway as depicted in (Scheme I.35). Thus in the present case CSI attacks at two positions, namely C_3 and C_4. The intermediate product thus obtained (under the influence of an acid catalyst) undergoes a cyclisation reaction leading to the final compound (109).

TABLE

Flavanone (g)	Products: m.p. (% yield)	
	I	II
2.93	183°(60)	282°(57)
3.07	190°(58)	285°(61)
3.23	195°(59)	270°(63)
3.53	187°(56)	276°(66)

I : formed by acid hydrolysis.

II : formed by alkaline hydrolysis.

Synthesis of 109 : Yield: 0.175g (60%), m.p. 183°.

Calcd for $C_{17}H_{10}NO_4$: C: 52.7; H: 4.0; N: 5.12

Found : C: 52.2; H: 3.2; N: 5.42%

IR spectrum (KBr) ν_{max} : 1780 ($\nu_{C=O}$).

PMR spectrum (DMSO-d_6), δ ppm : 6.2 (s, 1H, O-C<u>H</u>-C_6H_5), 6.8-7.7 (m, 9H, aromatic + 1H, NH).

Mass spectrum : m/z: 293 (M^+).

Synthesis of 110 : Yield: 0.178g (58%), m.p. 190°.

Calcd for $C_{18}H_{13}NO_4$: C: 70.35; H: 4.23; N: 4.56

Found : C: 70.46; H: 4.36; N: 4.39%

IR spectrum (KBr) ν_{max} : 1785 ($\nu_{C=O}$) cm^{-1}.

PMR spectrum (DMSO-d_6), δ ppm : 2.4 (s, 3H, C<u>H</u>$_3$), 6.3 (s, 1H, O-C<u>H</u>-C_6H_5), 7.1-7.8 (m, 8H, aromatic + 1H, NH).

Mass spectrum : m/z: 307 (M^+).

Synthesis of 111 : Yield: 0.190g (59%), m.p. 195°.

Calcd for $C_{18}H_{13}NO_5$: C: 66.87; H: 4.02; N: 4.33

Found : C: 66.71; H: 4.23; N: 4.12%

IR spectrum (KBr) ν_{max} : 1790 ($\nu_{C=O}$) cm^{-1}.

PMR spectrum (DMSO-d_6), δ ppm : 6.7 (s, 3H, OC<u>H</u>$_3$), 6.2 (s, 1H, O-C<u>H</u>-C_6H_5), 7.0-7.9 (m, 8H aromatic + 1H, NH).

Mass spectrum

Synthesis of 112 : Yield: 0.197g (56%), m.p. 187

Calcd for $C_{19}H_{15}NO_6$: C: 70.30; H: 4.62; N: 4.32

Found : C: 70.22; H: 4.49; N: 4.50%

IR spectrum (KBr) ν_{max} : 1780 ($\nu_{C=O}$) cm^{-1}.

PMR spectrum (DMSO-d_6), δ ppm : 3.7 (s, 3H, OCH_3), 3.8 (s, 3H, OCH_3), 6.4 (s, 1H, O-CH-C_6H_5), 6.8-7.1 (m, 7H aromatic + 1H,

Mass spectrum : m/z: 353 (M^+).

Synthesis of 113 : Yield: 0.187g (57%), m.p. 282°.

Calcd. for $C_{16}H_{11}NO_5S$: C: 58.35; H: 3.34; N: 4.25

Found : C: 58.18; H: 3.10; N: 4.42%

IR spectrum (KBr) ν_{max} : 1680 ($\nu_{C=O}$), 1380, 1170 (ν_{SO_2}) cm

PMR spectrum ($CDCl_3$), δ ppm : 6.3 (s, 1H, O-CH-C_6H_5), 6.9-7.8 (m, 9H aromatic), 9.2 (bs, 1H, NH).

Mass spectrum : m/z: 329 (M^+).

Synthesis of 114 : Yield: 0.209g (61%), m.p. 285°.

Calcd for $C_{17}H_{13}NO_5S$: C: 59.47; H: 3.79; N: 4.08

Found : C: 59.23; H: 3.86; N: 4.14%

IR spectrum (KBr) ν_{max} : 1675 ($\nu_{C=O}$), 1385, 1180 (ν_{SO_2}) cm^{-}

PMR spectrum ($CDCl_3$), δ ppm : 2.4 (s, 3H, CH_3), 6.4 (s, 1H, O-C<u>H</u>-C_6H_5), 6.8-7.9 (m, 8H aromatic), 9.1 (bs, 1H, NH).

Mass spectrum : m/z: 343 (M^+).

Synthesis of 118 : Yield: 0.226g (63%), m.p. 270°.

Calcd for $C_{17}H_{13}NO_6S$: C: 56.82; H: 3.62; N: 3.89

Found : C: 56.69; H: 3.81; N: 3.67%

IR spectrum (KBr) ν_{max} : 1685 ($\nu_{C=O}$), 1375, 1180(ν_{SO_2})cm

PMR spectrum ($CDCl_3$), δ ppm : 3.8 (s, 3H, OCH_3), 6.4 (s, 1H, O-C<u>H</u>-C_6H_5), 6.8-7.7 (m, 8H aromatic), 9.3 (bs, 1H, NH).

Mass spectrum : m/z: 359 (M^+).

Synthesis of 116 : Yield: 0.256g (66%), m.p. 276°.

Calcd for $C_{18}H_{15}NO_7S$: C: 55.52; H: 3.85; N: 3.59

Found : C: 55.43; H: 3.93; N: 3.44%

IR spectrum (KBr) ν_{max} : 1680($\nu_{C=O}$), 1380, 1175(ν_{SO_2}) cm^{-1}.

PMR spectrum ($CDCl_3$), δ ppm : 3.7 (s, 3H, OCH_3), 3.8 (s, 3H, OCH_3), 6.2 (s, 1H, O-C<u>H</u>-C_6H_5), 6.9-7.7 (m, 7H aromatic), 9.2 (bs 1H, NH).

Mass spectrum : m/z: 389 (M^+).

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CHAPTER II-A

REACTIONS OF 4-STYRYL-1,2,3-BENZOXATHIAZINE-2,2-DIOXIDES WITH VARIOUS ENAMINES

The reactions of 1(a-f) with various enamines were carried out. Out of the five enamines employed in the present investigation, the reactions of 1-pyrrolidino-1-cyclohexene and 1-piperidino-1-cyclo-hexene with 1(a-f) are most interesting. These reactions constitute a versatile method for the syntheses of the novel-bridged heterocyclic systems. The structures of these compounds have been elucidated on the basis of their elemental analysis, IR, PMR and mass spectral fragmentation data. ^{13}C-NMR spectral data for the afore-said compounds confirm the assigned structures explicitly. A plausible mechanism involving the participation of the solvent molecule, acetonitrile, has been postulated Other enamines, viz., 1-Morpholino-1-cyclohexene, 1-pyrrolidino-1-cyclopentene and 1-piperidino-1-cyclopentene have been found to undergo [4+2]cyclo-addition reaction[32,33] with 1(a-f), to afford the heterocyclic systems 9(a-f), 10(a-f), 11(a-f) respectively. These structures have been distinguished from their corresponding regio-isomers on the basis of PMR data.

The reactions of dichloro-ketene are well documented in literature.[1,2] Thus dichloro-ketene, generated from dichloroacetyl-chloride, has been found to undergo [2+2] addition reaction with C=N of (1a)

to furnish the heterocyclic system (12). These structures were arrived at on the basis of their spectral data.

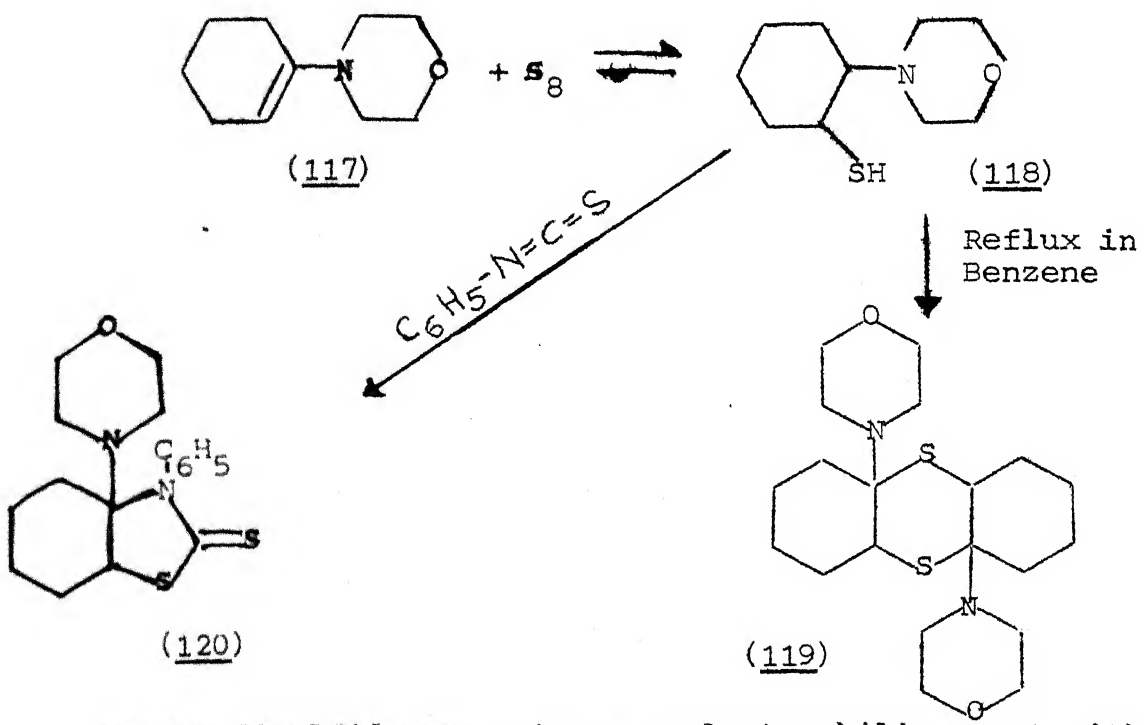
INTRODUCTION

4-Styryl-1,2,3-benzoxathiazine-2,2-dioxides were first synthesized in our laboratory,[3] by the reactions of 2'-hydroxy-chalcones and chlorosulfonyl isocyanate, in refluxing toluene. These compounds contain C=C and C=N in conjugation. The presence of SO_2 moiety in 1(a-f) makes it an electron deficient heterodiene system. These compounds undergo bromination smoothly with molecular bromine and epoxidation across the C=C bond with alkaline hydrogen peroxide.

Compounds 1(a-f) form an interesting class of substrates towards the addition reactions with 1,3 dipoles, for example, diazomethane, dichloro-ketene and enamines. In the present investigation, 4-styryl-1,2,3-benzoxathiazine-2,2-dioxide, carrying different substituents (viz., chloro, bromo, methyl and methoxy) in the styryl moiety were reacted with various enamines. The enamines employed in these cycloaddition reactions include, 1-pyrrolidino-1-cyclohexene, 1-piperidino-1-cyclohexene, 1-pyrrolidino-1-cyclopentene, 1-morpholino-1-cyclohexene and 1-piperidino-1-cyclopentene. The various cycloaddition reactions of enamines have been reported in the literature.

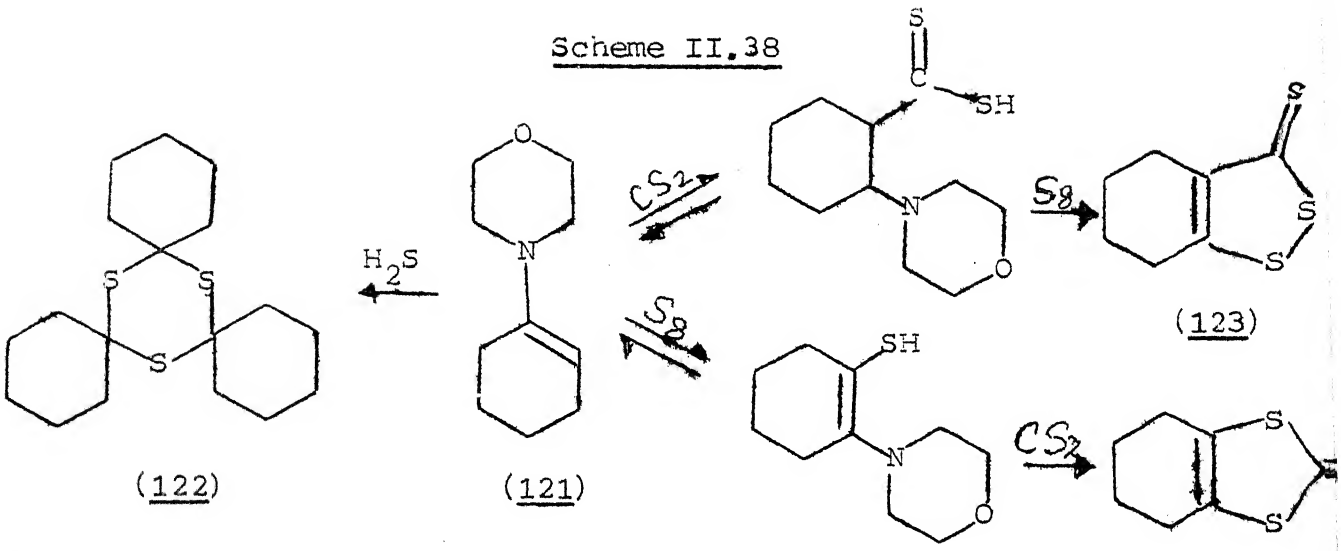
The nucleophilic attack of elemental sulfur takes place on the β-position of an enamine, (117), to yield thiolated intermediate (118). When the later compound is treated with phenyl isothiocyanate, the cyclic adduct (120) is formed.[4] Refluxing the morpholine enamine of cyclohexanone, (117), and elemental sulfur in benzene (solvent) results in the formation of hydrogenated thianthrene[5], (119).

Scheme II.37



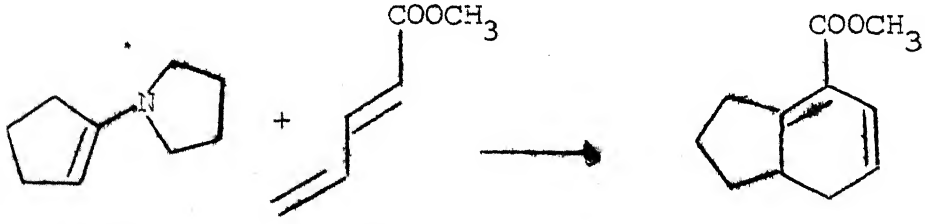
Carbon disulfide can act as an electrophilic agent with enamines, at room temperature. Therefore, the treatment of an enamine with elemental sulfur and carbon disulfide, in a polar solvent, results in the formation of a 3H-1,2-dithiole-3-thione (123) and 2H-1,3-dithiole-2-thione (124) respectively.[6]

Scheme II.38



(122) (121) (123)

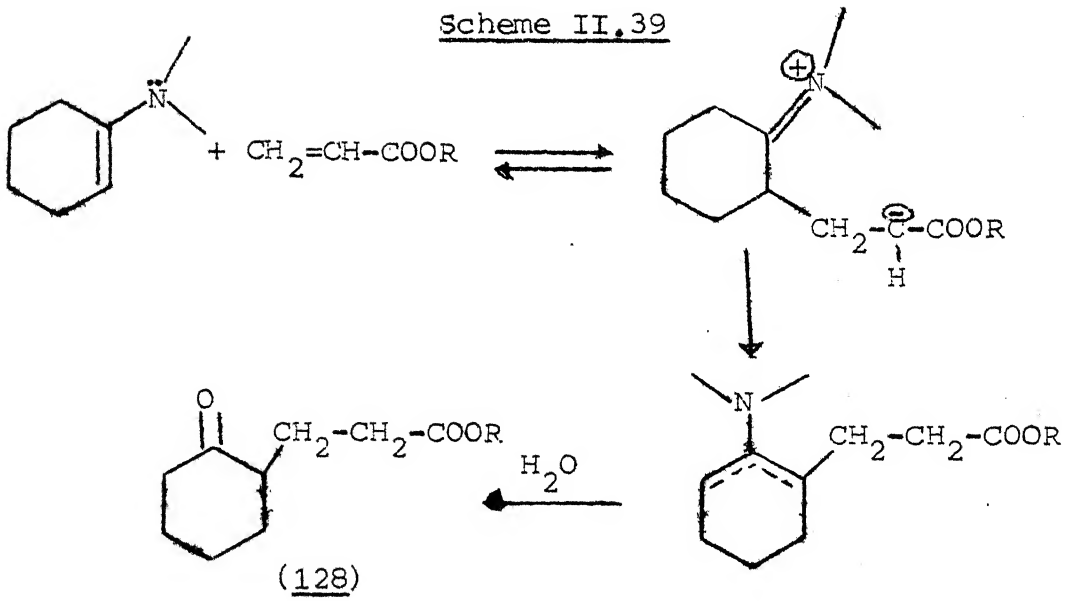
The use of enamines as intermediates, in organic syntheses has been extensively investigated. The electron-deficient diene, for example, methyl trans-2,4-pentadienoate (126) reacts with enamine to give the 1,4-cyclo-adduct (127) in a good yield.



(125) (126) (127)

Stork and coworkers[9] demonstrated the ability of electrophilic olefines to undergo nucleophilic attack with enamines. A typical overall process is shown as follows:

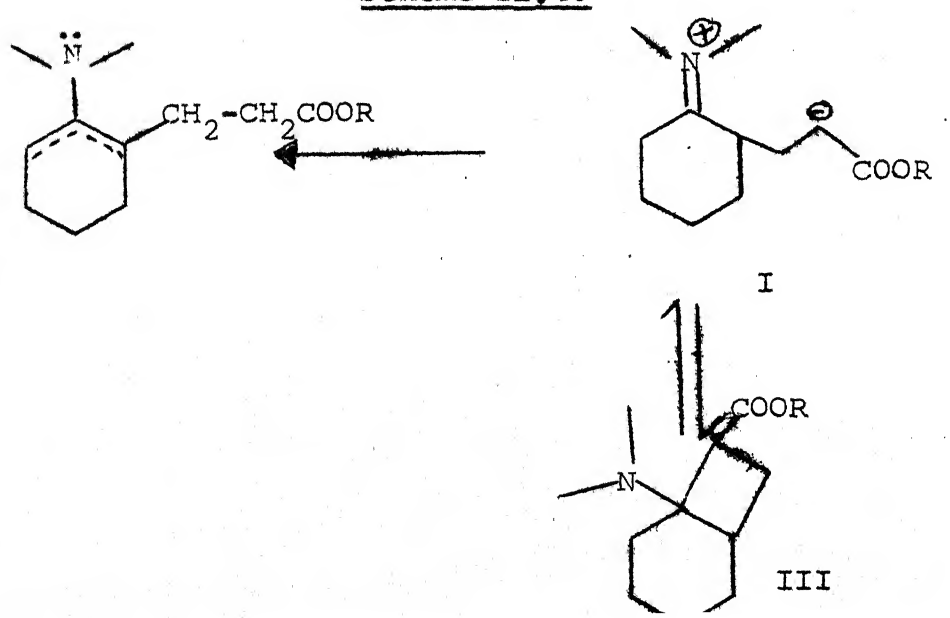
Scheme II.39



(128)

Brannock and coworkers[19] found that, under appropriate conditions, cyclobutane derivatives of the type III may be obtained. It is not certain whether they arise from direct cycloaddition or via a two-step (Michael-Mannich sequence). It would appear that III could well be in equilibrium with I (Mannich-retro-Mannich), an equilibrium which is presumbaly irreversibly displaced toward II by proton transfer.

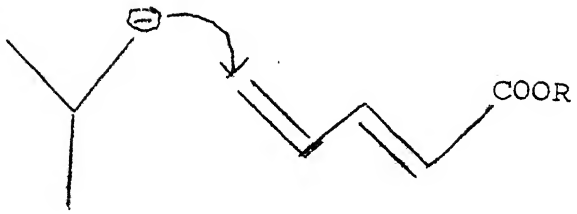
Scheme II.40



I

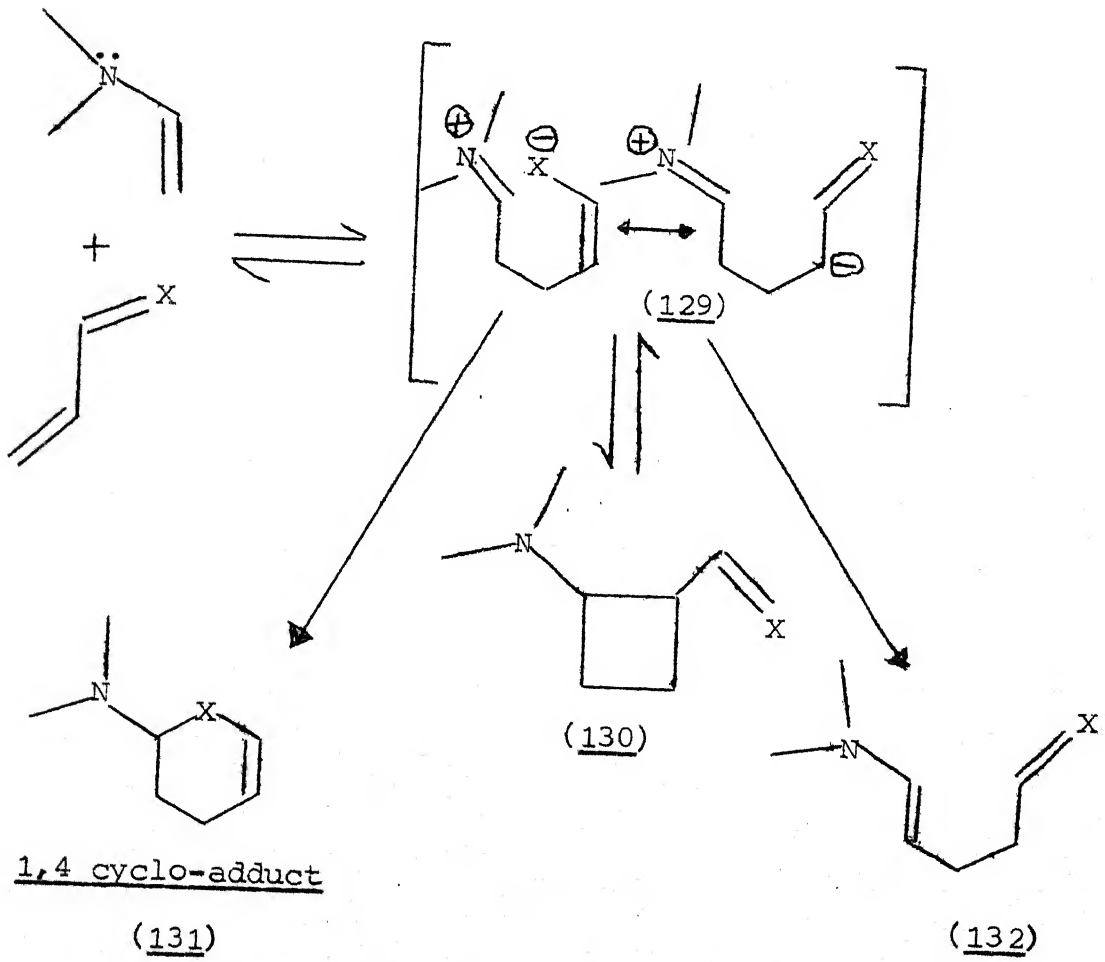
III

Derivatives of β-vinyl acrylates are well known to undergo 1,6-addition.

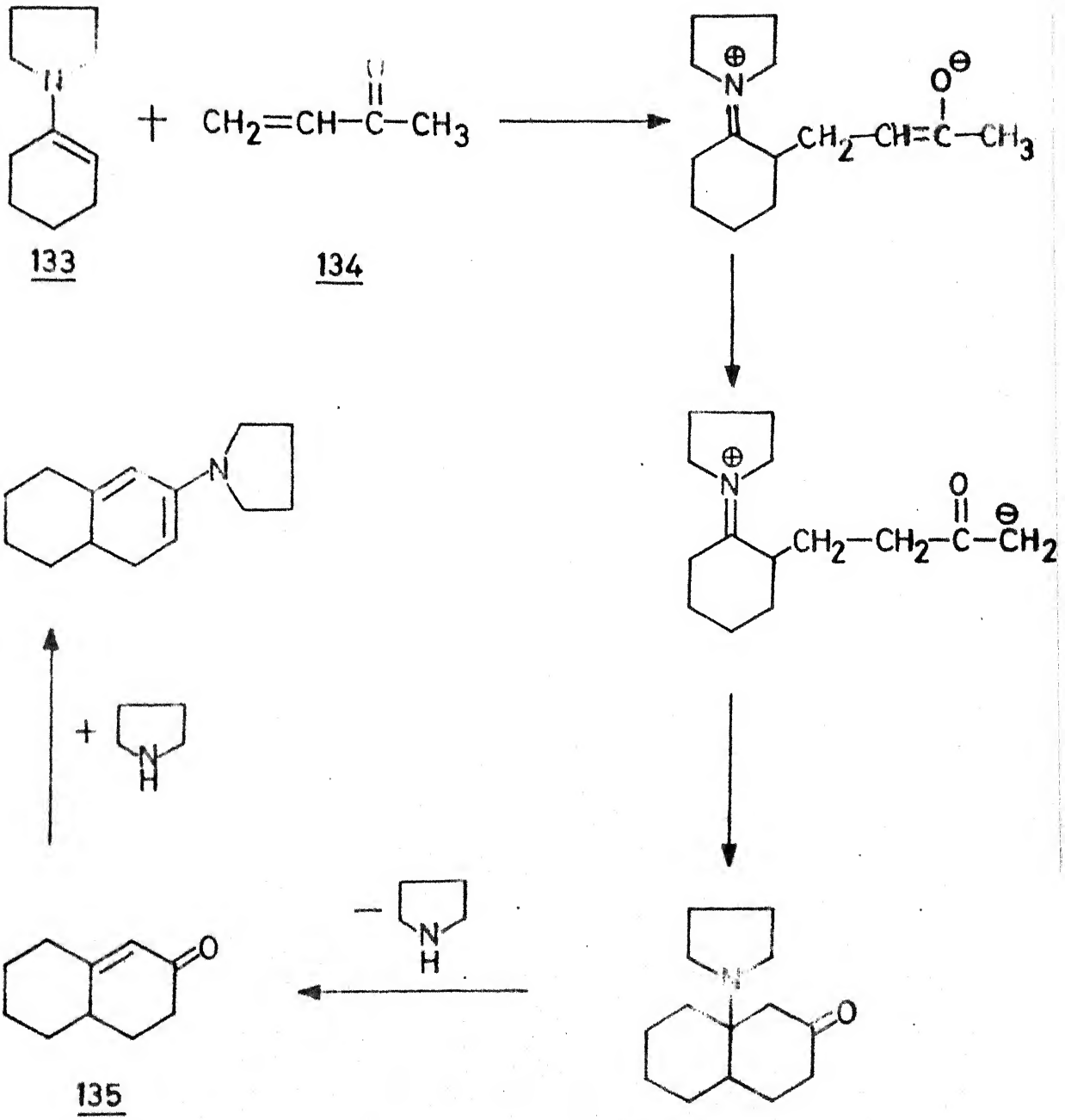


The alkenes carrying electron withdrawing substituents react with enamines to give alkylated 1,5-diene (132), 1,2 and 1,4 cycloaddition products (130, 131).

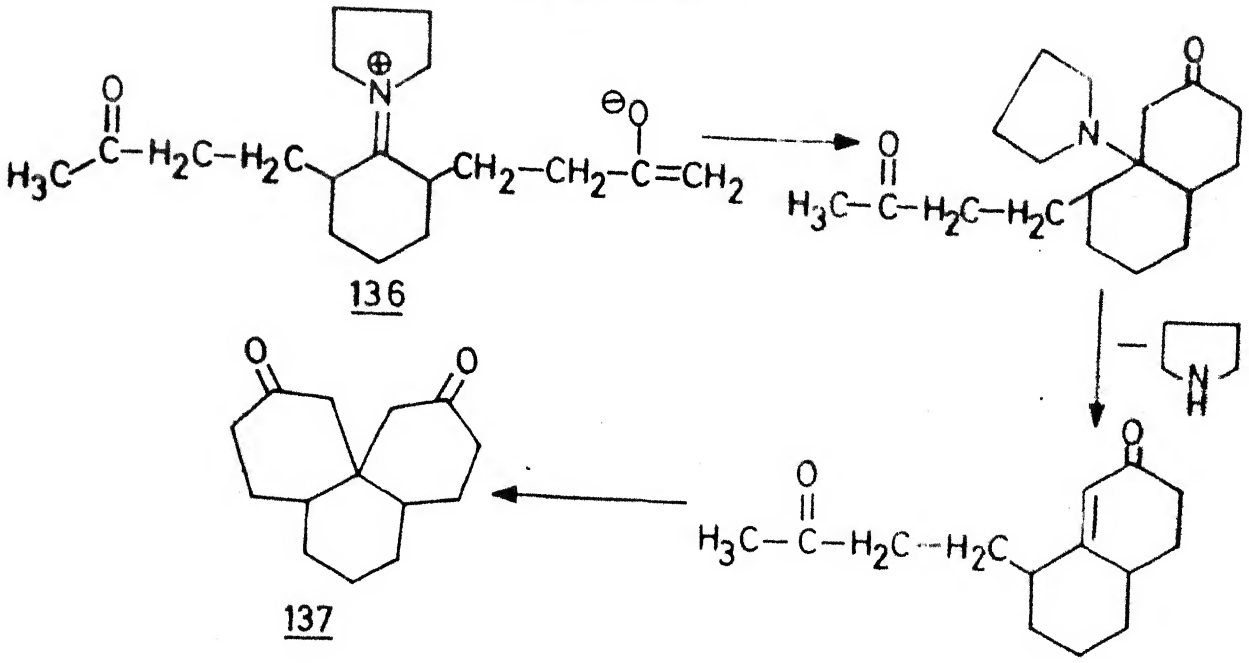
Scheme II.41



Scheme II.42



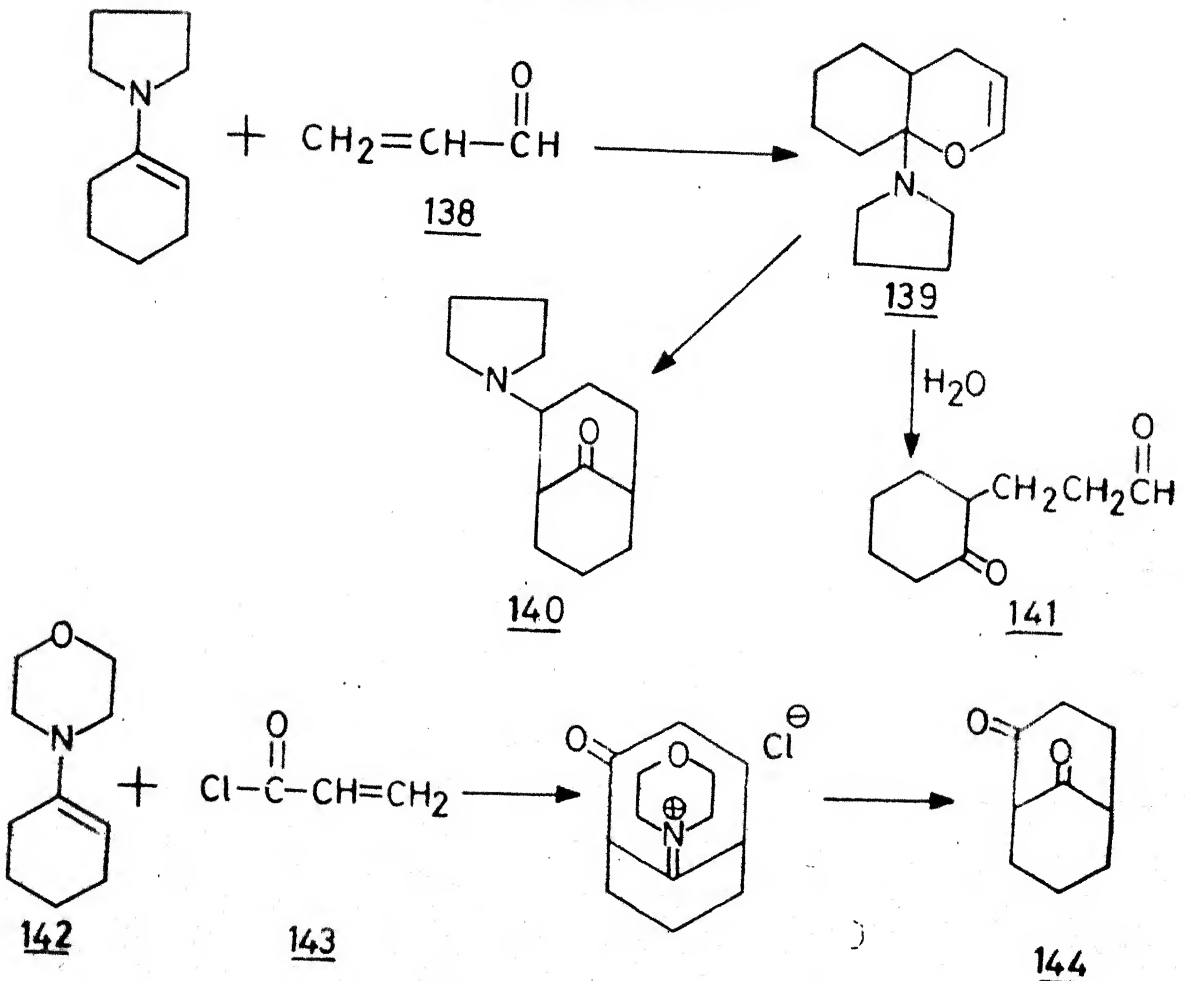
Scheme II.43



136

137

Scheme II.44



138

139

140

141

142

143

144

A step-wise ionic mechanism leading to these products, necessarily involves the formation of a zwitterion intermediate, (129) as the first step. This is then followed either by one of the two possible cycloadditions to give a cyclic molecule or proton-elimination addition[7,8] to give a simple alkylated molecule. The first reported cyclization involving an enamine was the 1,4-cyclo-addition of methyl vinyl ketone (134) with the enamine of cyclo-hexanone (133), to give, after hydrolysis, $\Delta^{1,9}$ octal-2-one[9] (135). The 1,4-cyclo-alkylation can be rationalized according to the mechanism depicted in Scheme II.42.

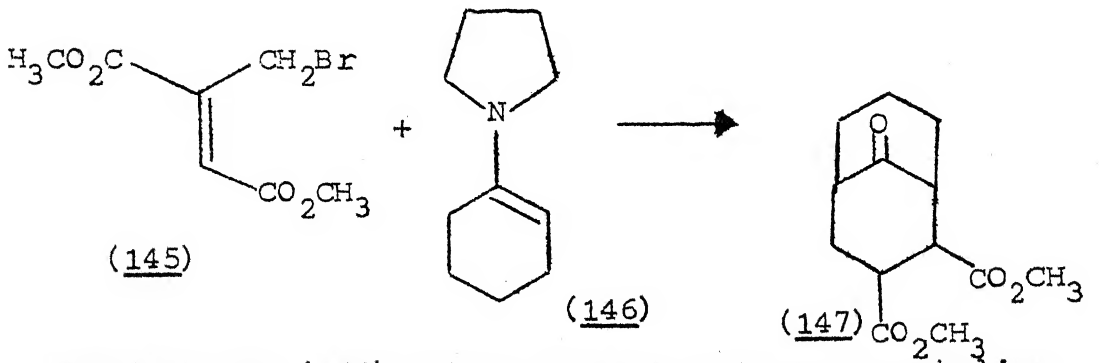
A by product diketone (137), was produced (before hydrolysis) in the above reaction. The yield of the diketone is reported[10] to increase either by substituting ethanol for benzene (as the reaction medium) or by omitting the solvent altogether. A plausible mechanism form the formation of the diketone from (136) is outlined in Scheme II.43.

Acrolein (138), when allowed to react with an enamine (such as pyrrolidine enamine of cyclohexanone) at room temperature, followed by distillation, gives an interesting bicycloaminoketone (140) in a 75% yield.[9] This reaction has proved to be a very useful method for ring expansion. The mechanism of this two step 1,3-cyclo-addition reaction was first studied by Untch.[11] For cyclo-hexanone enamines the initial product formed is dihydropyran (139).

On distillation (139) produces[12] bicycloamino ketone (140), while on hydrolysis it yields a ketoaldehyde (141).

A ring expanded product[13] (144) was secured by the interaction of 1-N-morpholino-1-cyclohexene (142) with acryloyl chloride (143). A two-step cyclization of an enamine with an electrophilic alkene has been reported.[14] In this reaction the first step is the alkylation by an allyl halide, followed by alkylation by the electrophilic alkene.[14] Thus, dimethyl bromomesconate (145) reacts with 1-(N-pyrrolidino)cyclohexene (146) to produce, after hydrolysis, a bicyclic keto-diester(147).

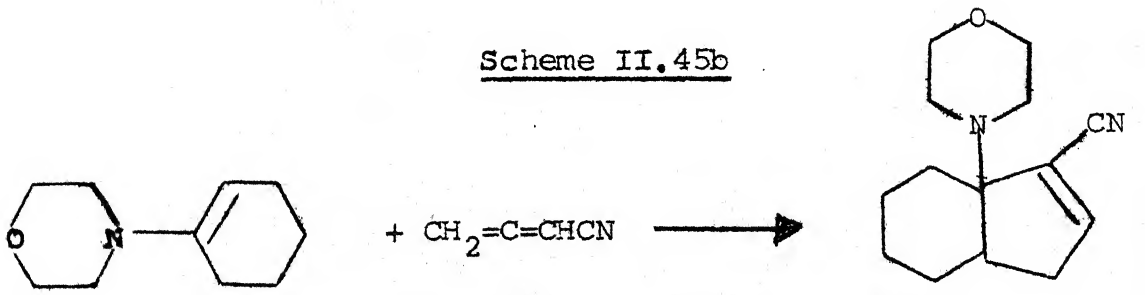
Scheme II.45a



(145) (146) (147)

Cyano-allene (148), when treated with the morpholine enamine of cyclohexanone is reported[15] to undergo a 1,3-cyclo-addition reaction to form (149).

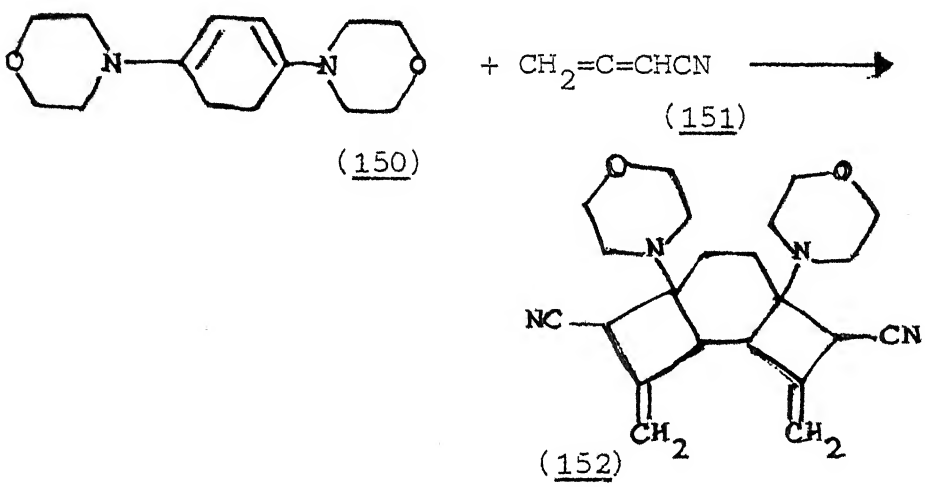
Scheme II.45b



(148) (149)

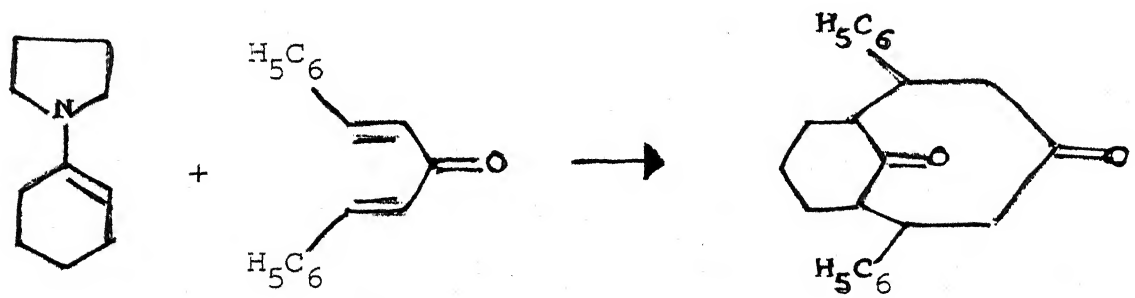
while, on the other hand, the cyano allene (148) reacts with diendiamine (150) to produce di-1,2-cyclo-addition adduct (152).

Scheme II.45C

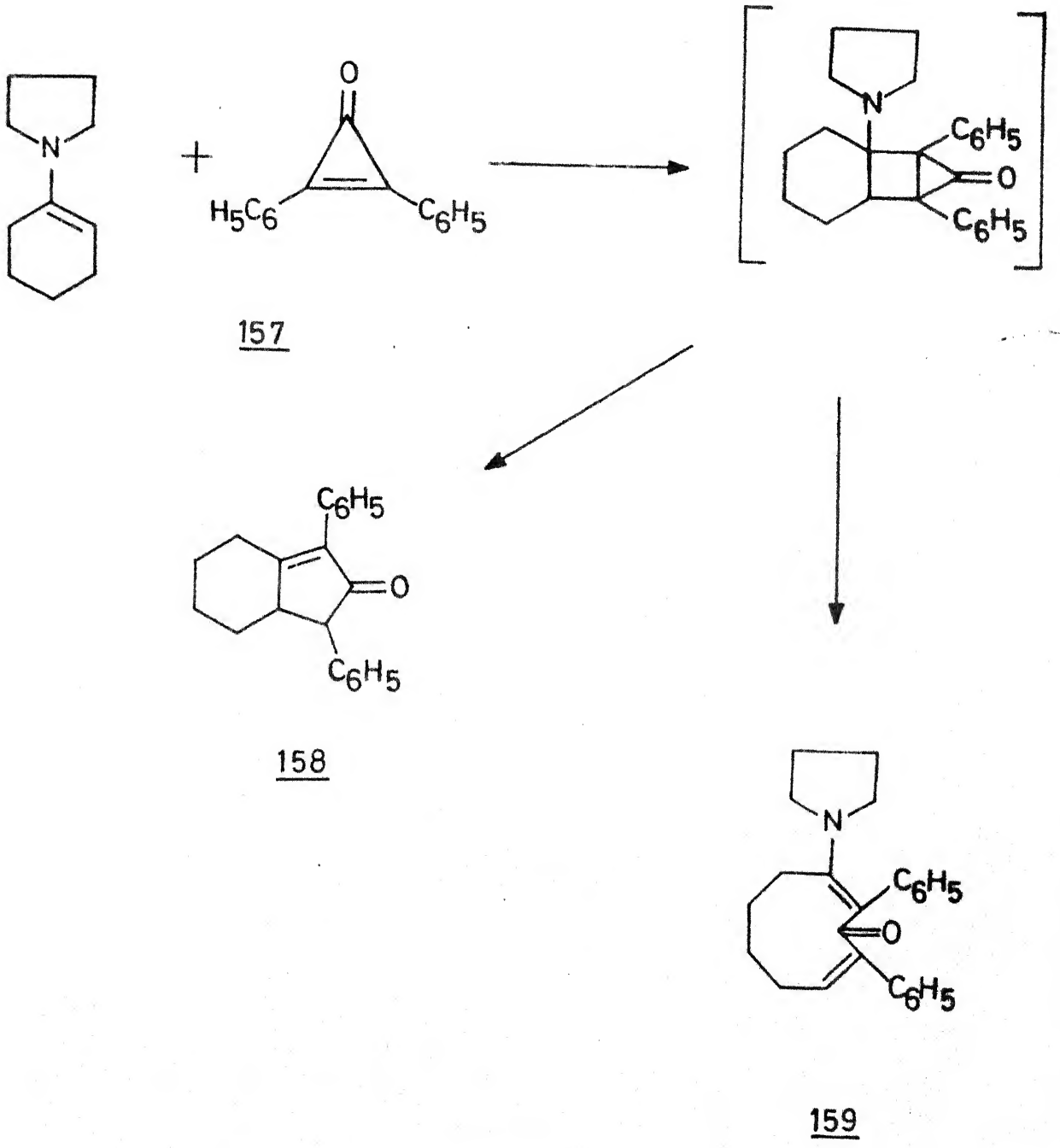


A conjugated ketone, viz., dibenzal acetone (153), is reported[16] to add to the pyrrolidine enamine of cyclohexanone to yield a bicyclo [5,3,1] undecane adduct (154).

Scheme II.46



Scheme II.47

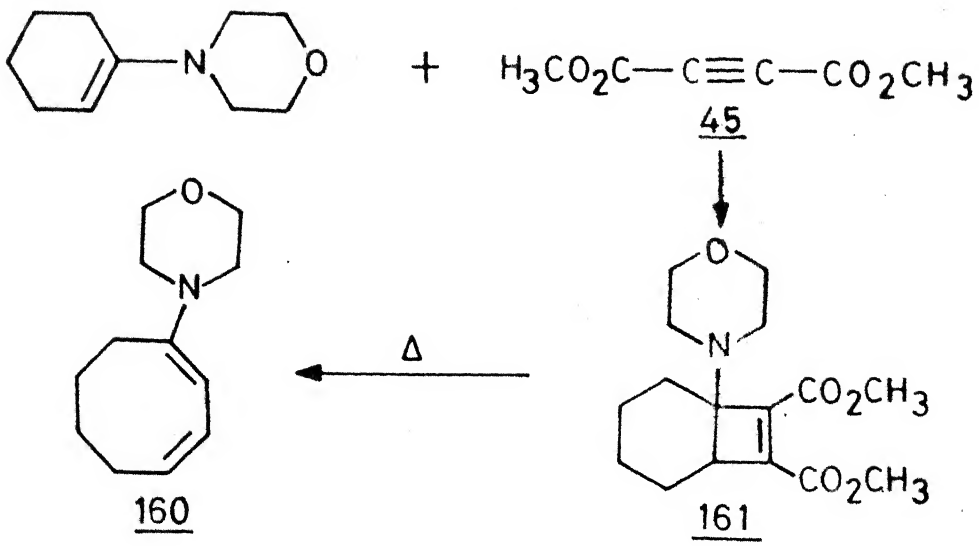


157

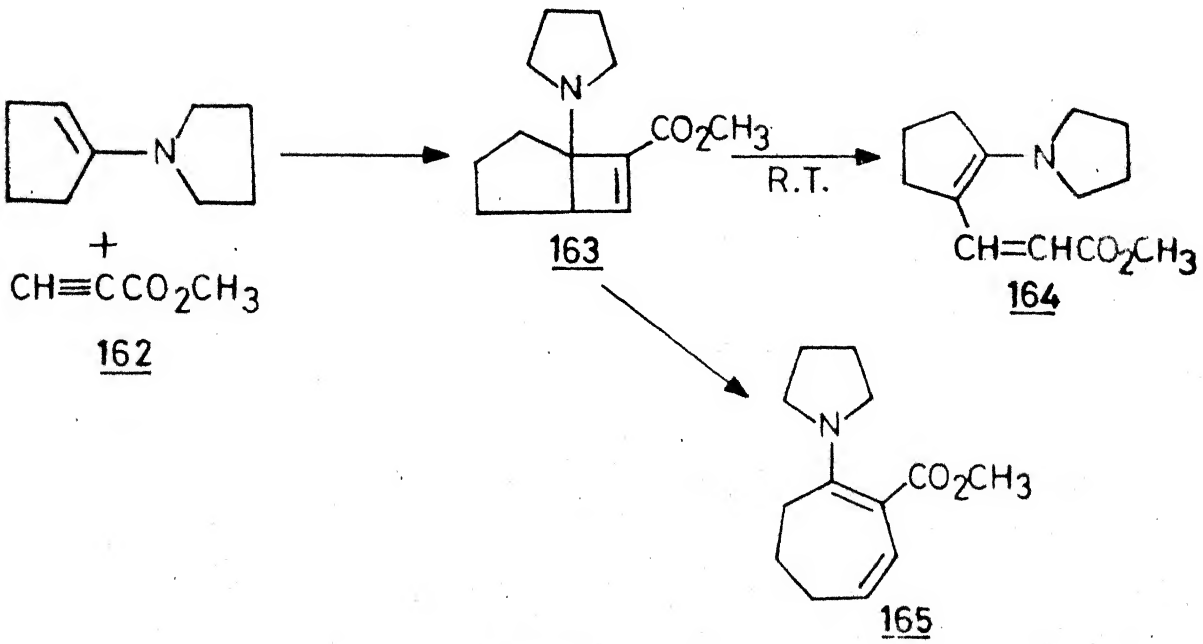
158

159

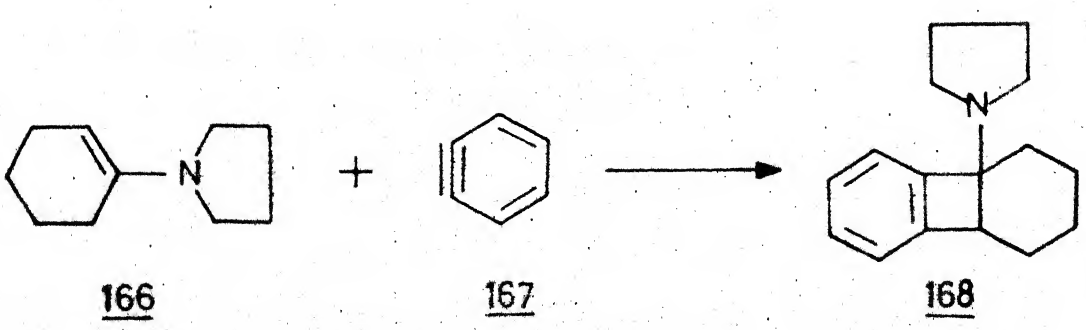
Scheme II.48a



Scheme II.48b

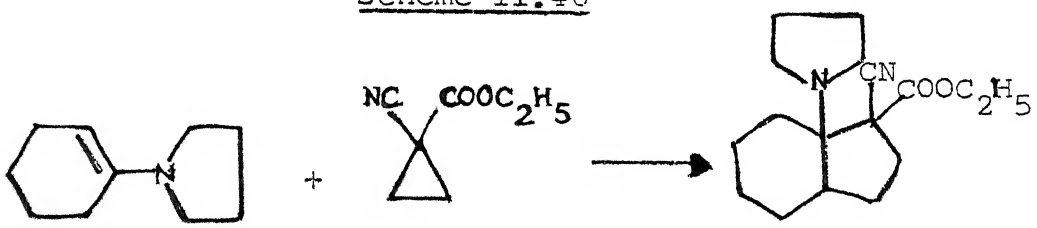


Scheme II.48c



1,3-Cycloaddition reaction occurs[17] when pyrrolidine enamine of cyclohexanone is reacted with cyclopropyl cyanoester, (155).

Scheme II.46



(155) (156)

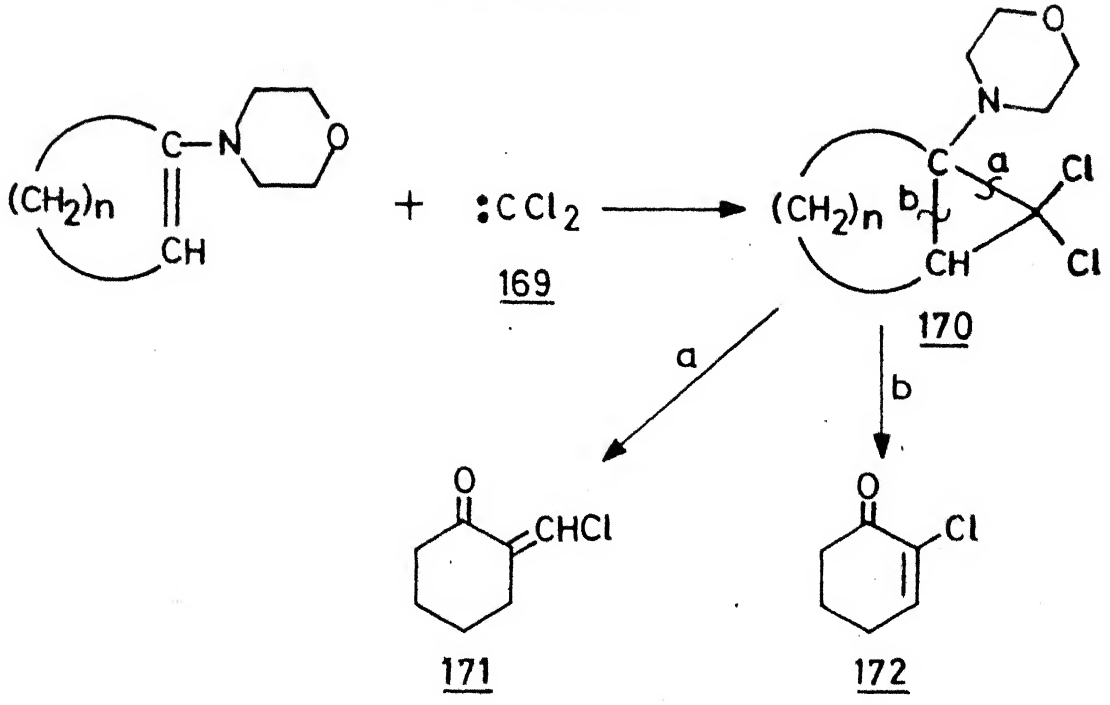
A similar reaction has been described in respect of the interaction of N-carbethoxy-aziridine, with the same enamine.

Diphenyl cyclopropenone (157), undergoes 1,2 cycloaddition with alicyclic enamines, followed by the breaking of sigma bonds in the intermediate[18] compound as shown in Scheme II.47.

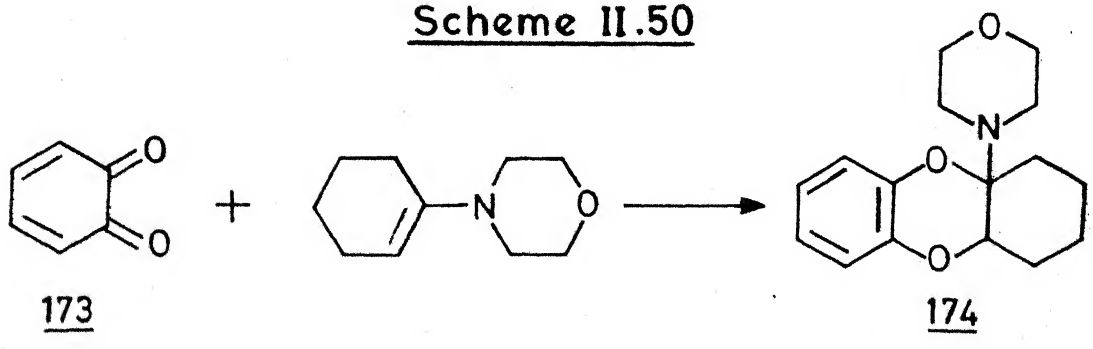
Terminal alkynes, with no electron withdrawing group adjacent to the acetylinic linkage, when treated with enamines merely add across the double bonds of the enamines.[19] Electrophilic alkynes (those with an electron withdrawing substituents adjacent to the acetylinic linkage), however undergo cycloaddition reactions with enamines.

Six-membered ring enamines produce stable cyclobutene adducts with dimethyl acetylene dicarboxylate, which then decompose upon heating into ring enlargement products. This is illustrated as shown in Scheme II.48.

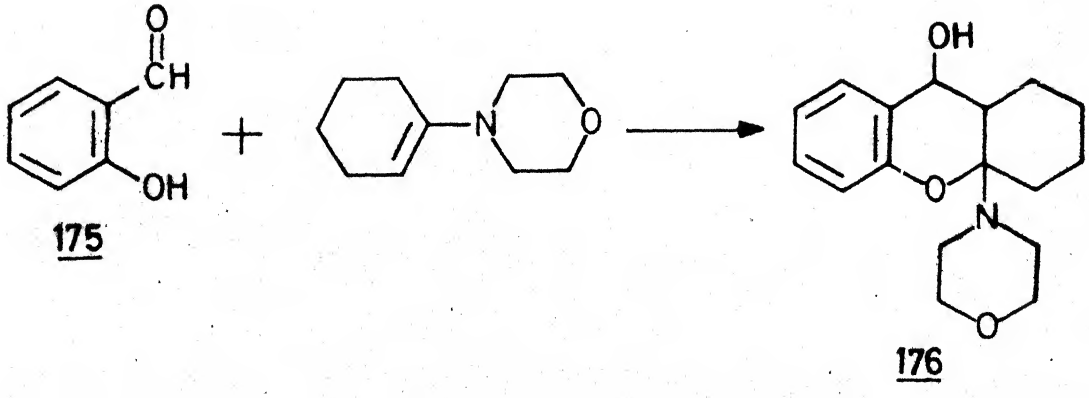
Scheme II.49



Scheme II.50



Scheme II.51



The pyrrolidine enamine of cyclopentanone forms stable 1,2 cycloaddition adduct(163) with methyl propiolate (162). Adduct(163) rearranges, upon standing at room temperature, to the simple alkylation product (164). However, the adduct (163) furnishes[20], a heptadiene derivative(165) upon heating.

The reaction of an alicyclic enamine with benzyne intermediate leads either to arylation or the formation of 1,2-cycloaddition products, depending upon the reaction conditions employed.[21] A typical example is illustrated in Scheme II.48c.

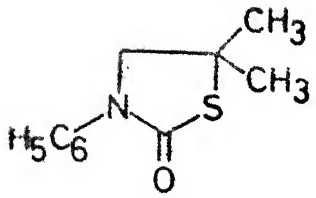
Addition of dichlorocarbene to the enamine of cyclohexanone gives a relatively stable adduct[22](170). Hydrolysis of the adduct causes cleavage, by pathway a, leading to the formation of the ketone (171). On the other hand cyclopentanone dichlorocarbene adduct produces a ring expanded product(172) by pathway b.

1,4-Cycloaddition is illustrated[23] by the reaction of o-quinone with the enamine derived from morpholine cyclohexanone (MCE), illustrated in Scheme II.50.

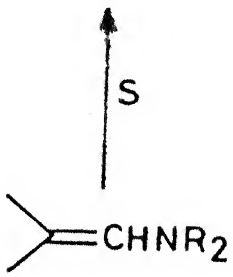
Another interesting example of 1,4-addition is that of salicylaldehyde with MCE, leading to the formation of a pyranol[24] in a quantitative yield (Scheme II.51).

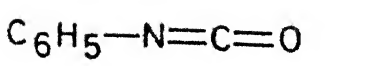
Enamines, lacking β-hydrogens, react, at room temperature, with phenyl isocyanate producing β-lactams.[25] The reaction presumably involves zwitterion intermediate (179). The formation

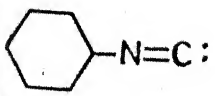
Scheme II.52



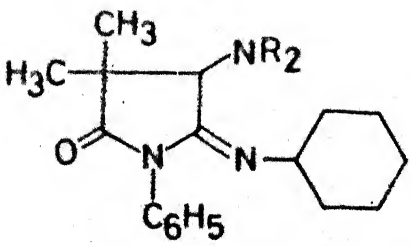
177



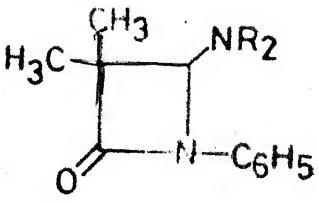




182

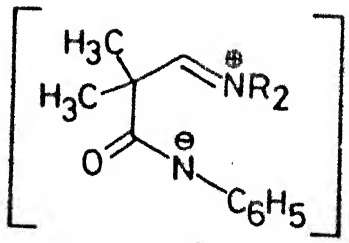


181

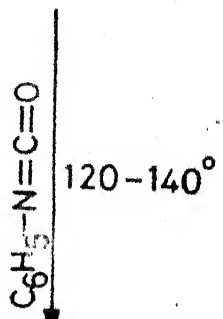


178

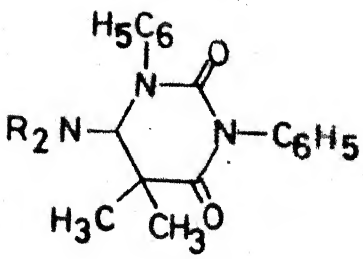
R.T



179



120-140°

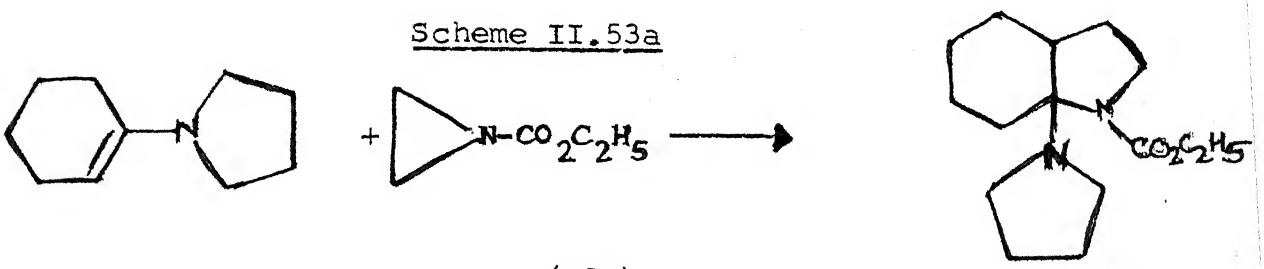


180

of 1,3-thiazolidin-2-one (177) has been reported[26], if the above reaction is carried out in presence of sulfur. These enamines have also been found to react with phenyl isocyanate (in presence of cyclohexylisonitrile) to produce pyrrolidones (181). It is interesting to note that (179) reacts at a higher temperature with another molecule of phenyl isocyanate, leading to the formation of amino hydro-uracil (180).

An analogous reaction has been reported[27] in respect of MCE with benzoyl isothiocyanate. Pyrrolidine enamine of cyclohexanone has successfully been reacted with N-carbethoxy aziridine (181), to produce octahydro indoles[28] (182).

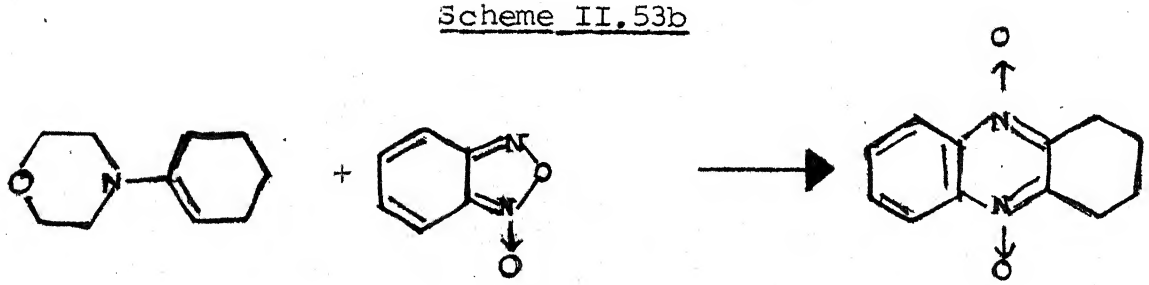
Scheme II.53a



(181) (182)

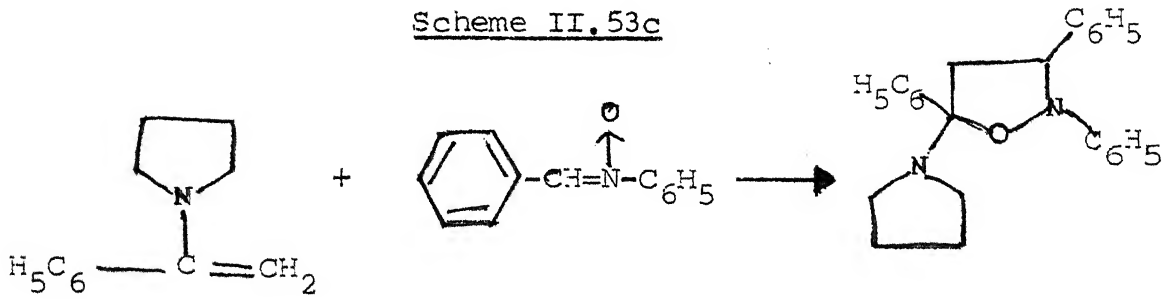
CME undergoes 1,4-cycloaddition with iso-benzofuroxan to form quinoxaline-di-N-oxide as shown (vide infra).

Scheme II.53b



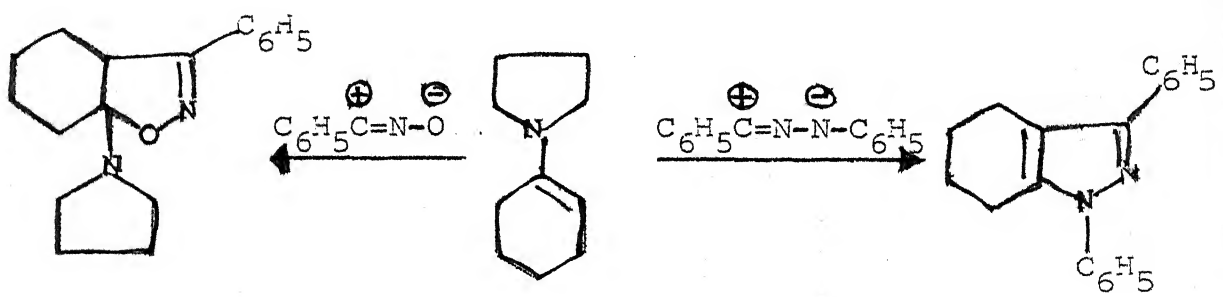
The preparation of isoxazolidine[29] is based on the cyclo-addition of nitrones to enamines. Thus:

Scheme II.53c



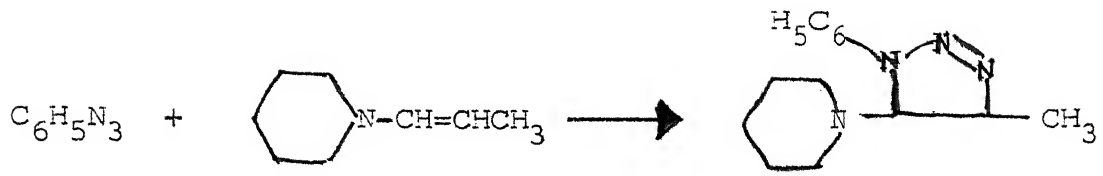
The 1,3-cycloaddition is typified by the interaction of enamines with nitrilimines and nitriloxide. These reactions provide good alternative methods for the preparation of pyrazoles[30] and isoxazoles[31] respectively.

Scheme II.54



A similar reaction of enamines with azides has been reported.[31]

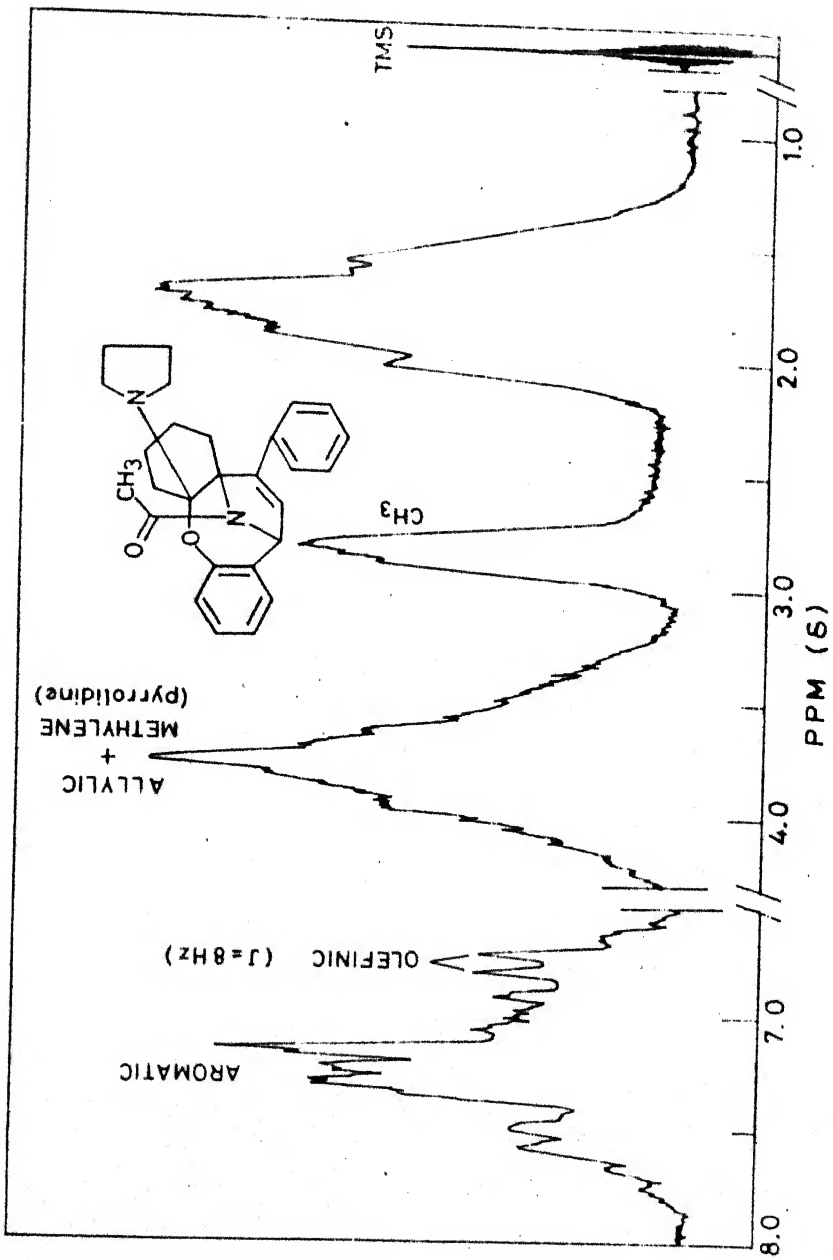
Scheme II.54

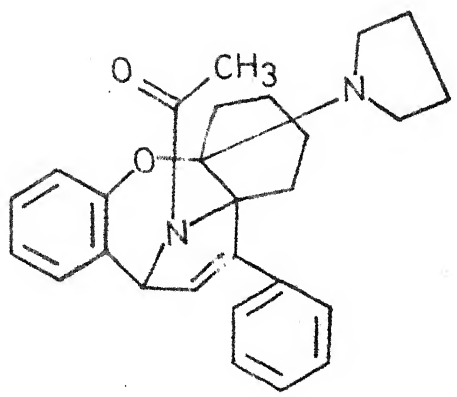


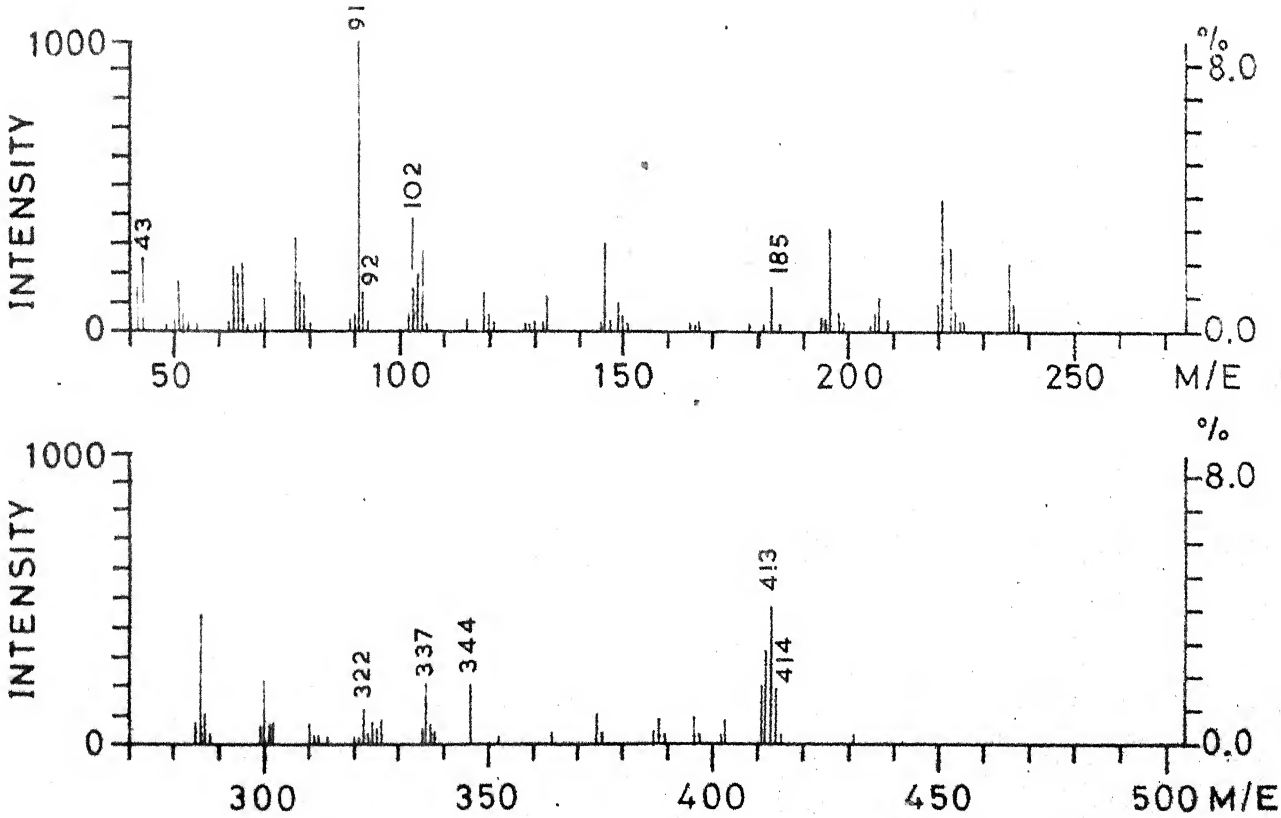
(183) (184) (185)

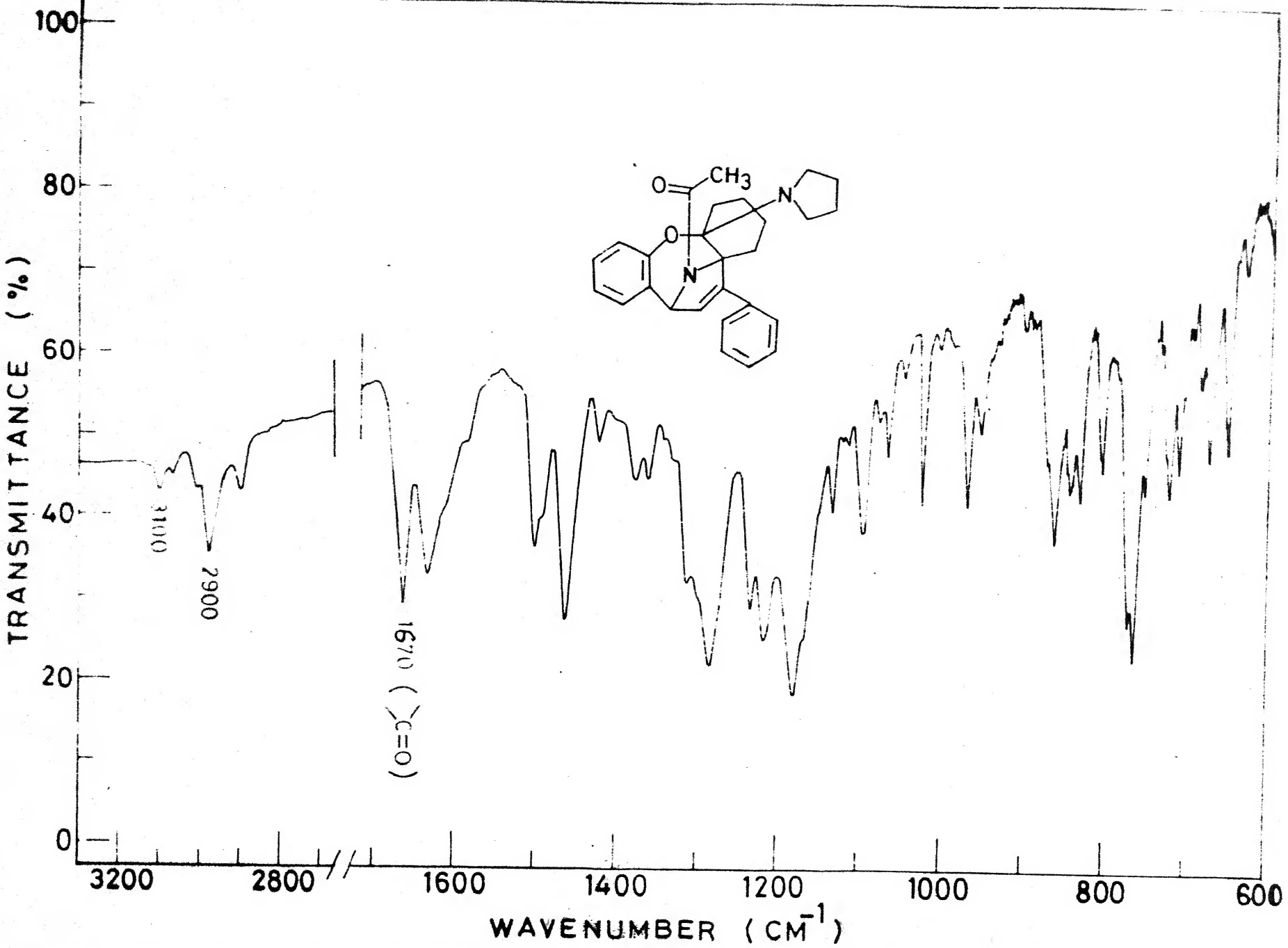
RESULTS AND DISCUSSION

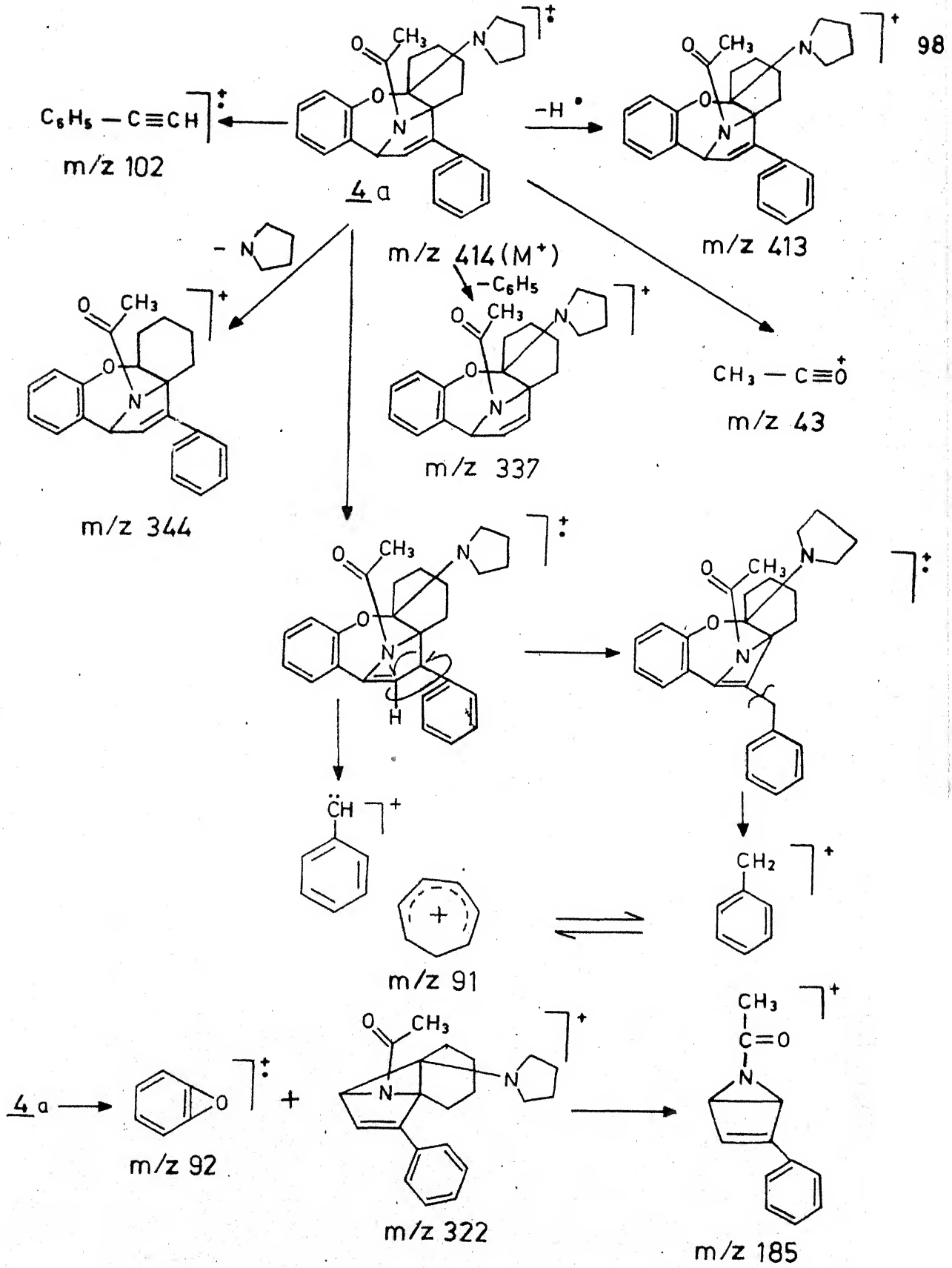
1a-f undergo smooth reaction with 1-pyrrolidino-1-cyclohexene 2 and 1-piperidino-1-cyclohexene (3), in acetonitrile at room temperature, to give compounds (4a-f) and (5a-f), in quantitative yields. The reactions were completed with in a few minutes and the products separated as white crystalline solids. The structures 4, 5(a-f) were established on the basis of IR, PMR and mass spectral data. The molecule does not contain a SO_2 group, is substantiated by the conspicuous absence of the IR bands at 1150 and 1370 cm^{-1} respectively. The strong absorption at ν 1670 cm^{-1} points to the presence of carbonyl function. The three methyl protons appear as a singlet at δ 2.8 in the PMR spectrum. The olefinic proton shows up as a doublet (J = 8 Hz) at δ 6.7. The allylic proton (along with the four methylene protons attached to the nitrogen atom of the pyrrolidine ring) shows as a complex multiplet centred at δ 3.8. The remaining protons appear as a

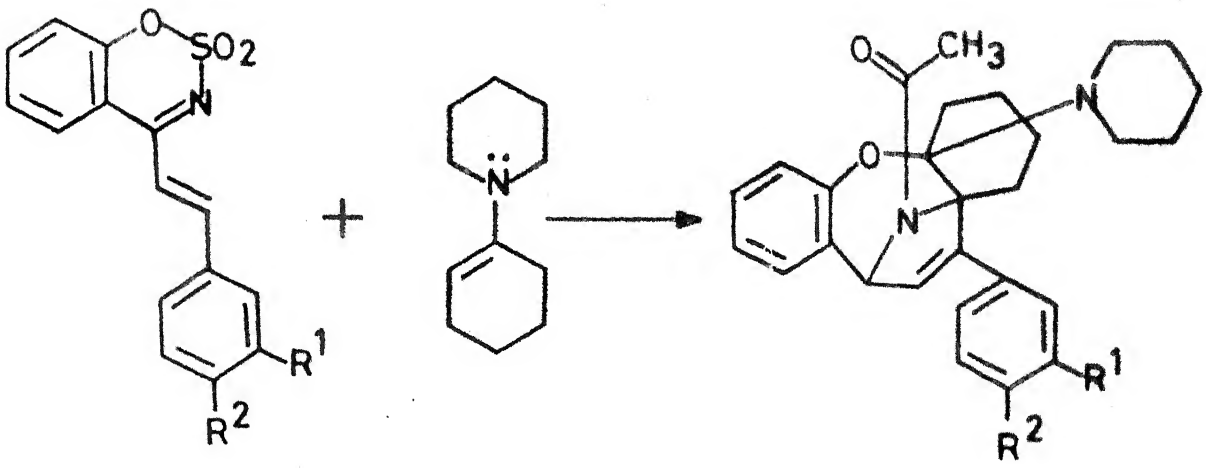

TMS
1.0
2.0
3.0
4.0
7.0
8.0
PPM (δ)
CH3
ALLYLIC
+
METHYLENE
(pyrrolidine)
OLEFINIC (J = 8 Hz)
AROMATIC
N
CH3
O
N
O


O
CH3
N
O
N


1000
INTENSITY
0
43
91
92
102
185
%
8.0
0.0
50
100
150
200
250
M/E
1000
INTENSITY
0
322
337
344
413
414
%
8.0
0.0
300
350
400
450
500 M/E

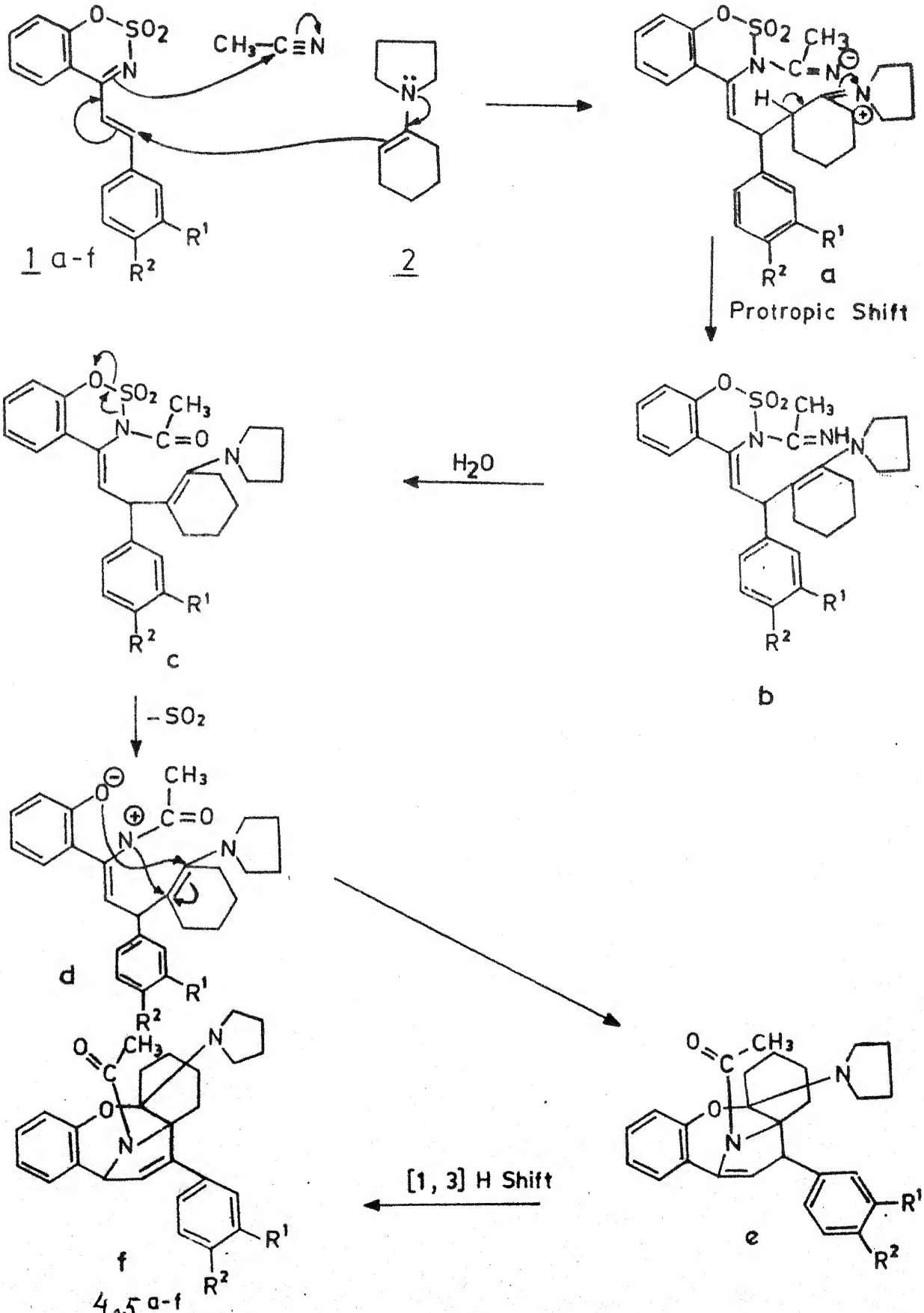

100
80
60
40
20
0
TRANSMITTANCE (%)
3100
2900
1691
(C=O)
3200
2800
1600
1400
1200
1000
800
600
WAVENUMBER (CM⁻¹)
O
CH3
N
O
N

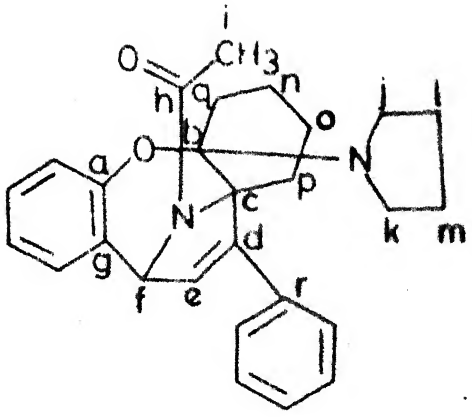

C6H5 — C≡CH
m/z 102
4a
m/z 414 (M+)
-H•
m/z 413
- N
-C6H5
m/z 337
CH3 — C≡O
m/z 43
m/z 344
m/z 91
m/z 92
m/z 322
m/z 185



1 a-f 3 5 a-f

4, 5	R^1	R^2
a	H	H
b	H	Cl
c	H	Br
d	H	CH_3
e	H	OCH_3
f	OCH_3	OCH_3
g	H	H
h	H	Cl
i	H	Br
j	H	CH_3
k	H	OCH_3
l	OCH_3	OCH_3


1 a-f
2
a
Protropic Shift
b
H_2O
c
$-SO_2$
d
e
[1, 3] H Shift
f
4,5 a-f



^{13}C-NMR (DMSO-δ_6) in δ (ppm)

a = 145.37
b = 105.83
c = 66.76
d = 141.78
e = 122.06
f = 70
g = 143
h = 153.12
i = 19.60
r = 135

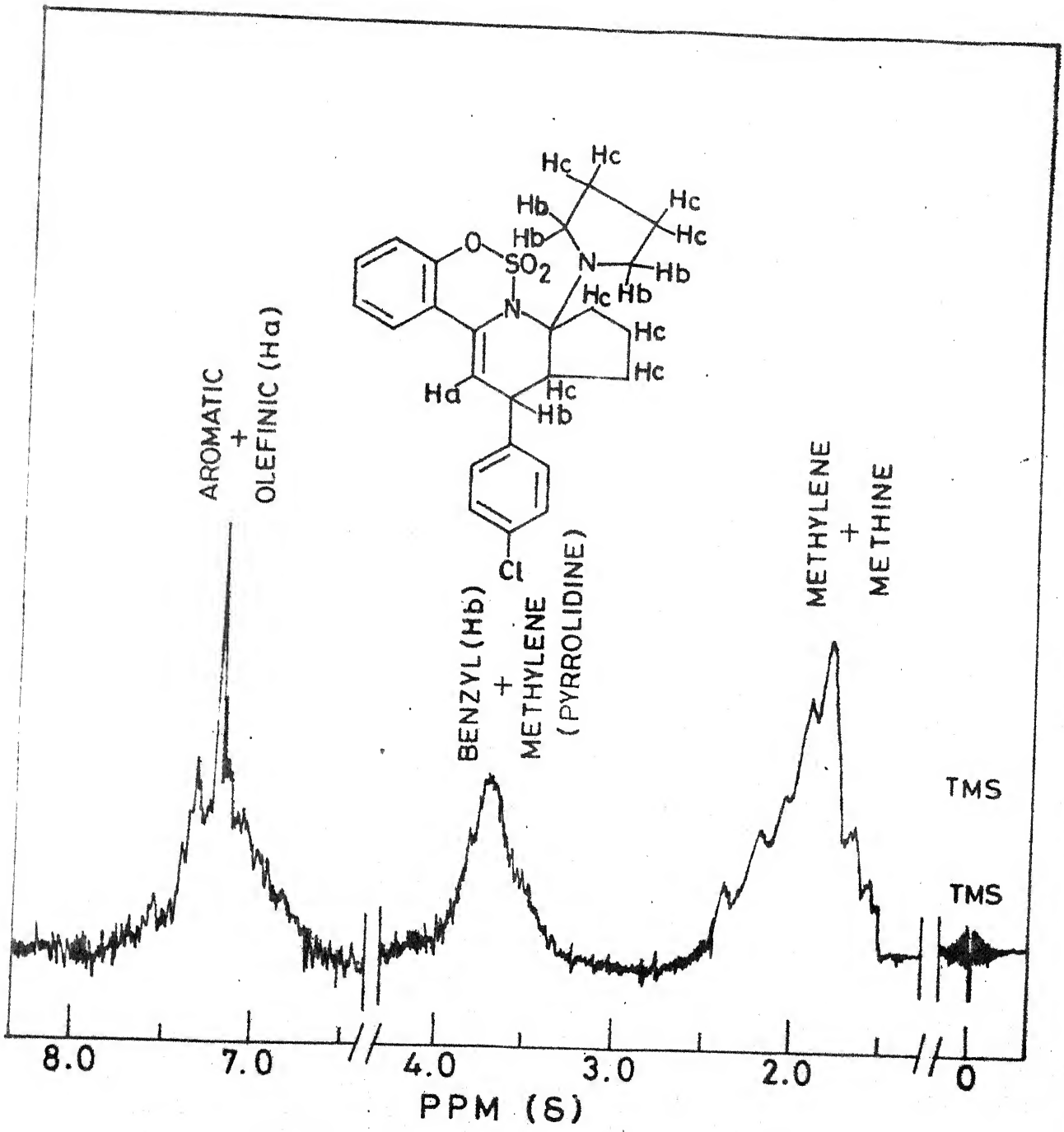
j, k, l, m (signals due to pyrrolidinium carbons)
= 45.08, 23.91, 23.80, 22.80

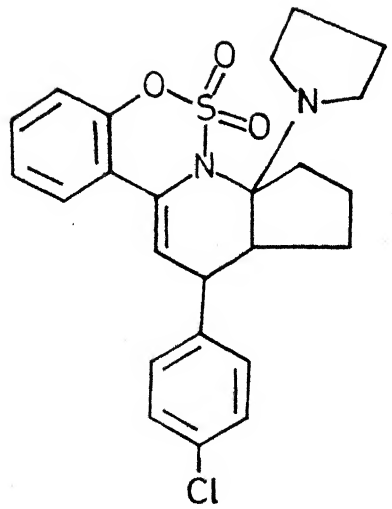
p, q, n, o (signals due to cyclohexane carbons)
= 59.49, 51.79, 30.57, 30.04

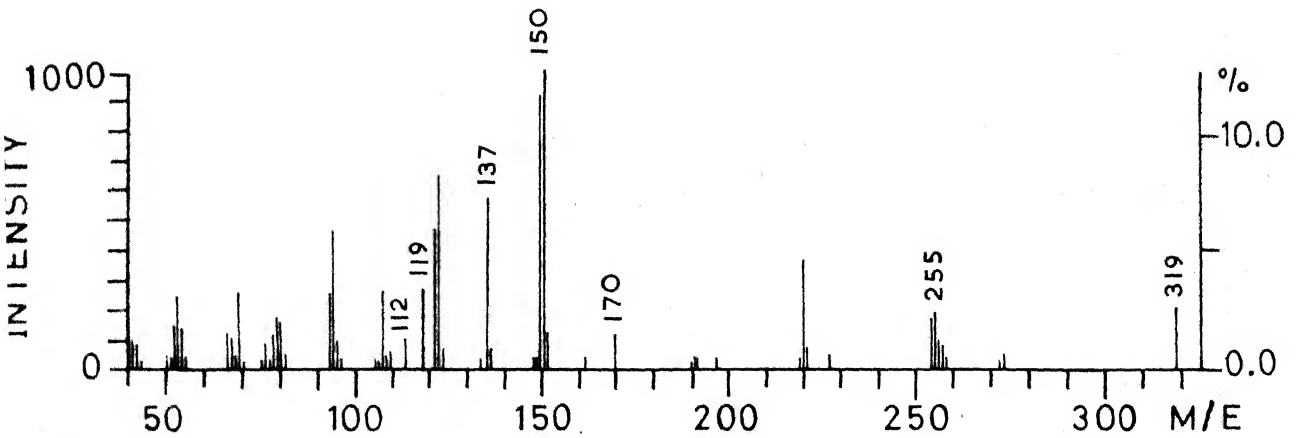
(signals due to aromatic carbons)
= (multiplet δ 121.18 - 128.41 ppm)

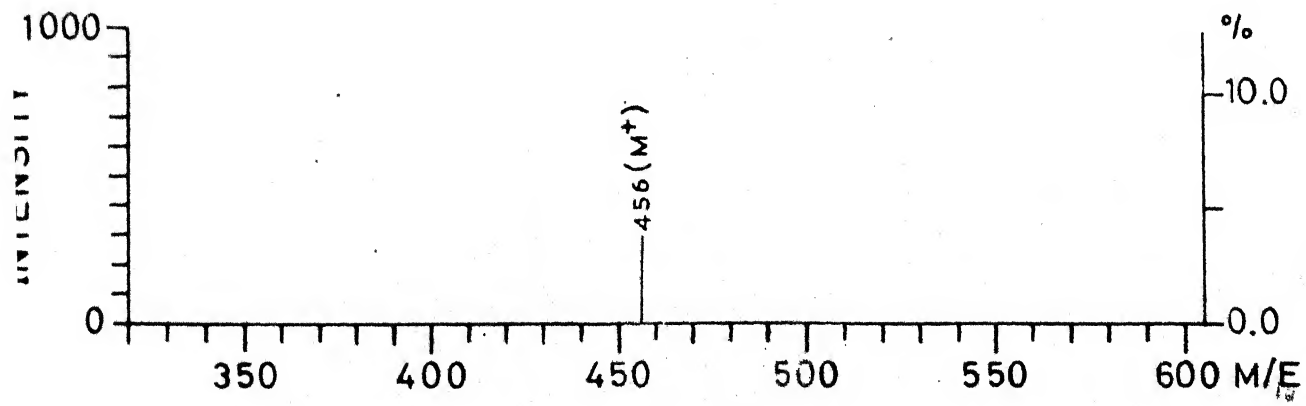
multiplet at δ1.7. The aromatic protons appear as a complex multiplet at δ7.2. The mass spectral data of the products confirm the assigned structures. The fragmentation pattern observed in the case of 4a is represented in page 96 . The mass spectrum of 4a exhibits molecular ion peak at m/z 414 and the fragmentation peaks at m/z 413 (M^+-H), 344 (M^+-N⬠), 337 (M^+-C_6H_5), 102 (C_6H_5-$C\equiv\overset{+}{C}H$), 91 (tropylium cation) respectively. A plausible mechanism for the formation of 4a has been postulated and is depicted on page 100.

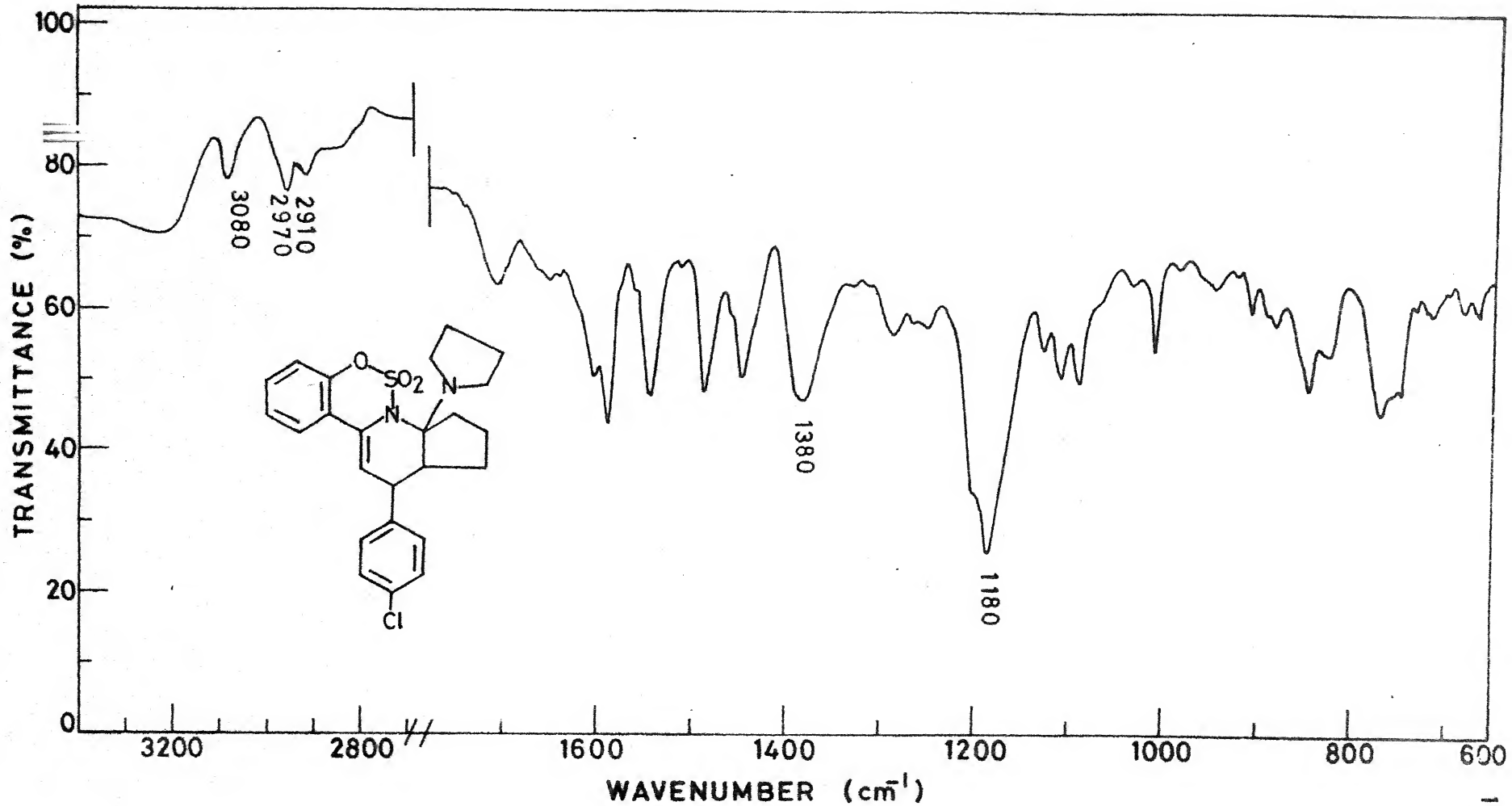
The first step is the nucleophilic addition of the enamine (2) to (1a). This is followed by the attack of electron pair of C=N bond of 4-styryl-1,2,3-benzoxathiazine-2,2-dioxide (1a) to the nitrile group of the solvent to give the dipolar intermediate (a). The product (b) is obtained by the appropriate prototropic shift of the intermediate (a) . The resulting imine (b), undergoes hydrolysis with the trace amount of water present in the solvent to give (c) . Elimination of SO_2 gives the zwitterion species (d) . It undergoes addition across the C=C bond to furnish the unstable (e) in accordance with the Bredt's Rule. 1,3 hydrogen shift in the intermediate leads to the formation of the product (f). It is interesting to note, that (4a) could not be isolated, if the solvent (acetonitrile) was replaced by dichloromethane, benzene or benzonitrile. This observation confirms that acetonitrile participates in the reaction. The hydrolytic step as envisaged

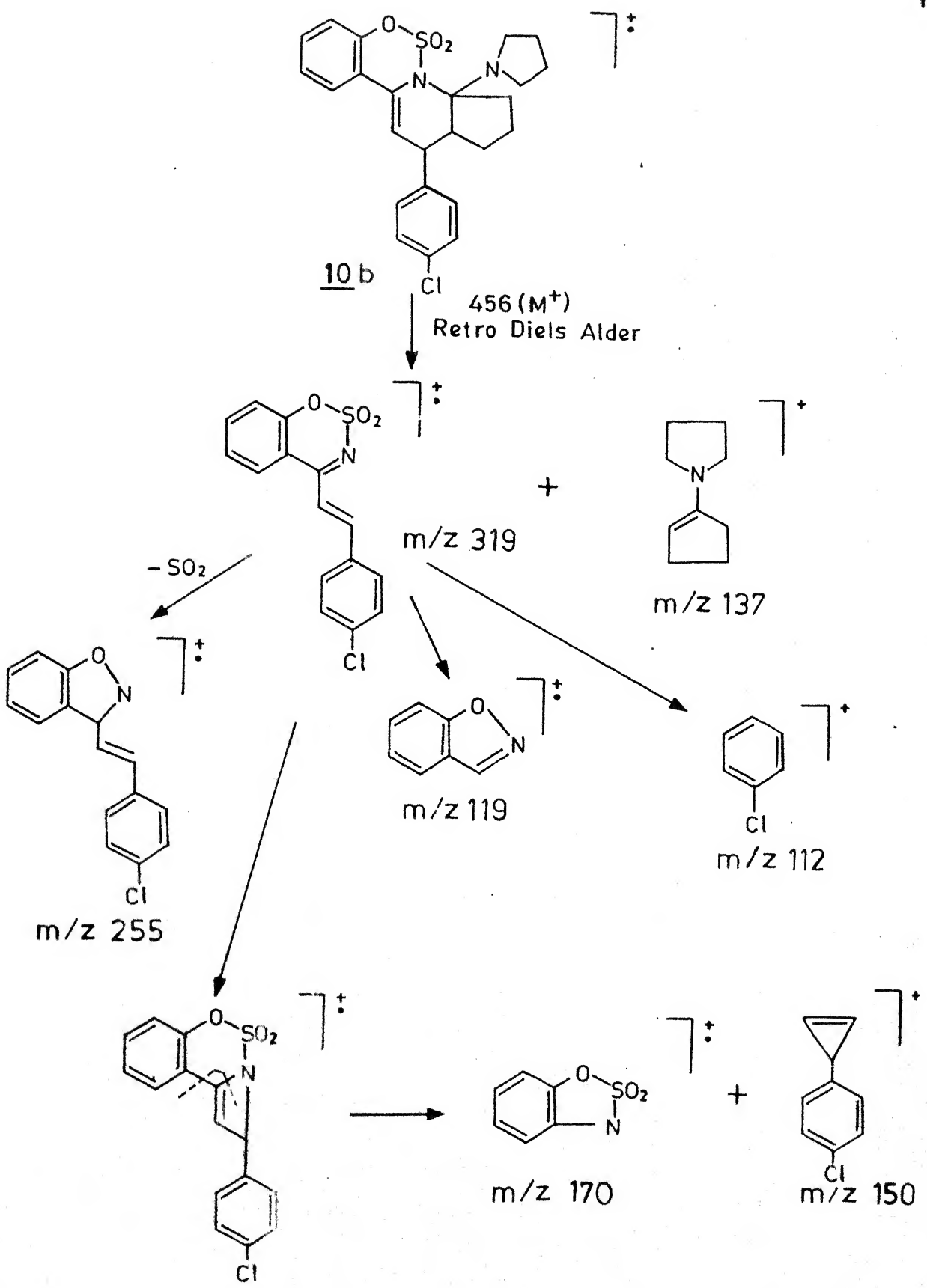

Hc Hc
Hb
Hc
Hb
Hc
O
SO2
N
Hb
Hc Hb
N
Hc
Hc
Ha
Hc
Hb
Cl
AROMATIC
+
OLEFINIC (Ha)
BENZYL (Hb)
+
METHYLENE
(PYRROLIDINE)
METHYLENE
+
METHINE
TMS
TMS
8.0
7.0
4.0
3.0
2.0
0
PPM (δ)

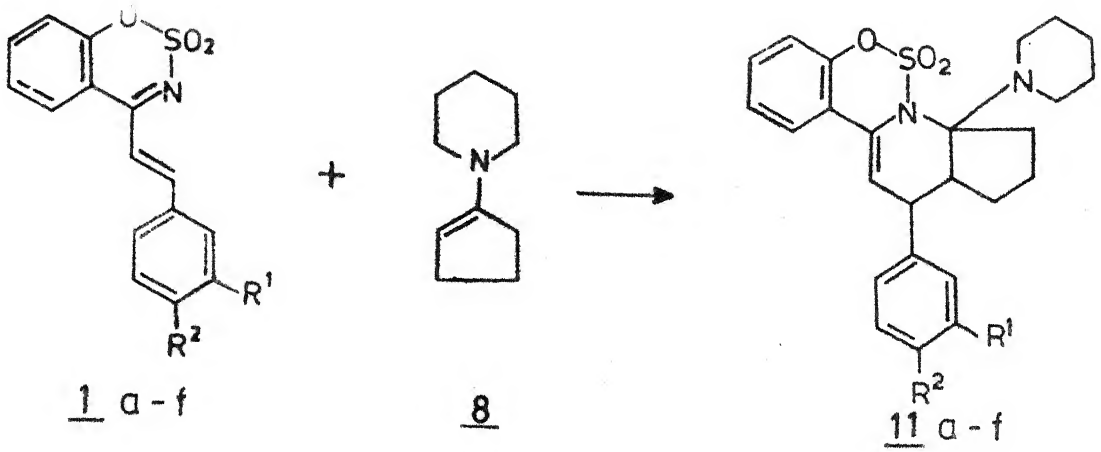

O
O
S
O
N
N
Cl


1000
0
INTENSITY
%
10.0
0.0
150
137
119
112
170
255
319
50
100
150
200
250
300
M/E

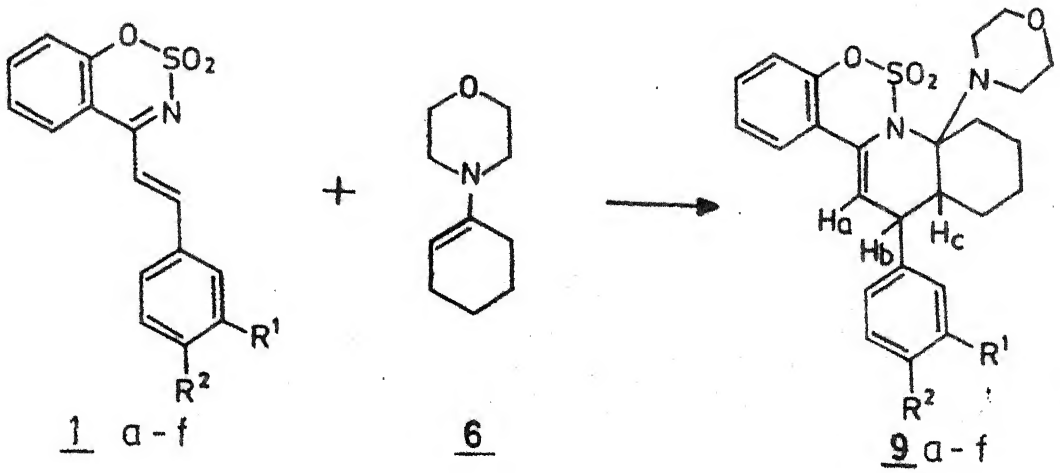

1000
0
%
10.0
0.0
456(M+)
350
400
450
500
550
600
M/E


100
80
60
40
20
0
TRANSMITTANCE (%)
3080
2910
2970
1380
1180
O
SO2
N
N
Cl
3200
2800
1600
1400
1200
1000
800
600
WAVENUMBER (cm-1)

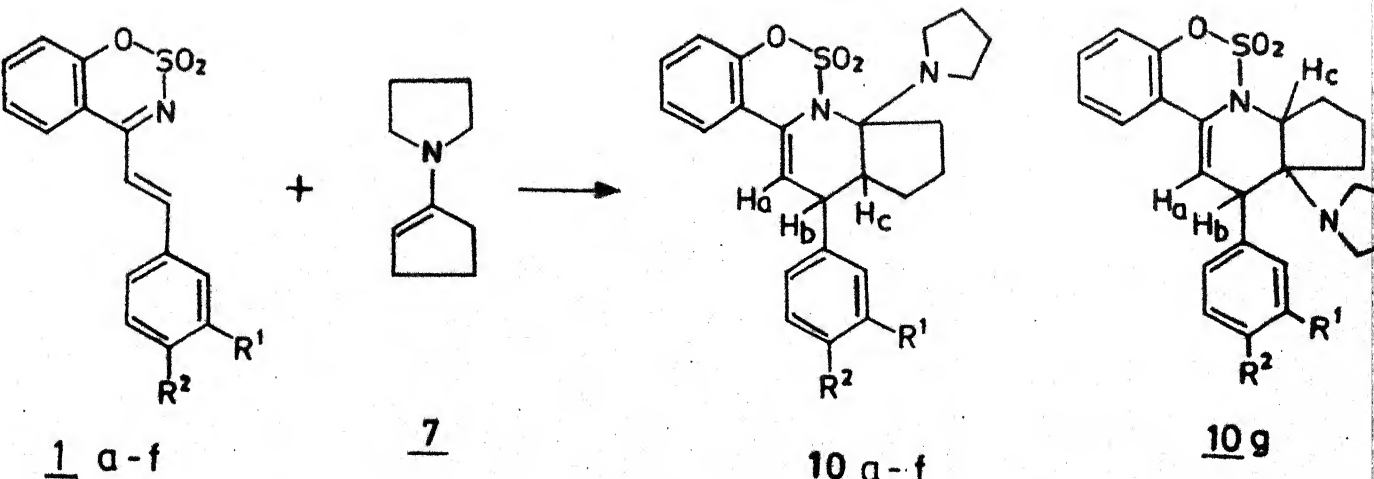

10 b
456 (M+)
Retro Diels Alder
m/z 319
m/z 137
m/z 255
m/z 119
m/z 112
m/z 170
m/z 150
Cl
N
O
SO2
- SO2



1 a - f + 8 → 11 a - f



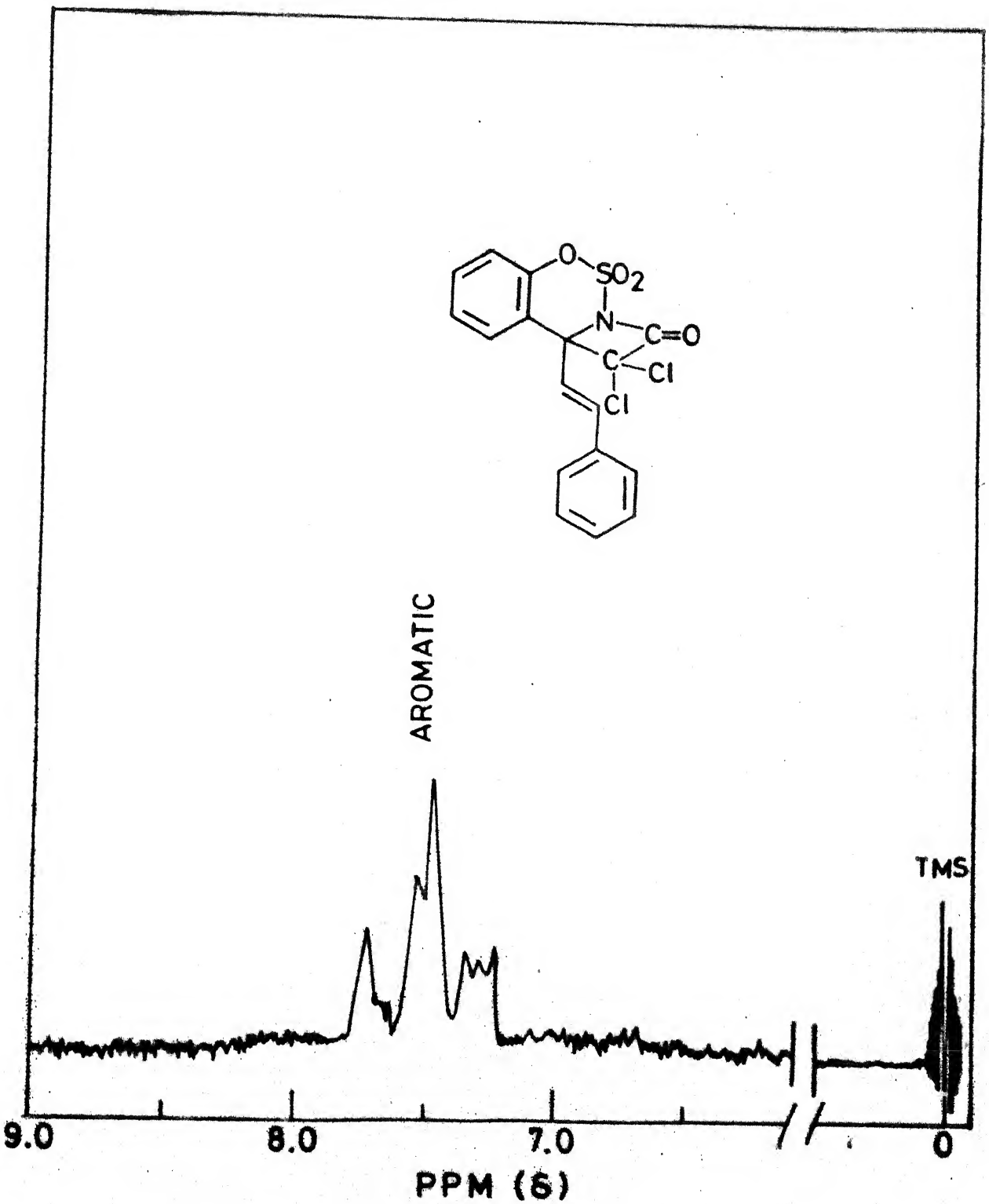
1 a - f + 6 → 9 a - f

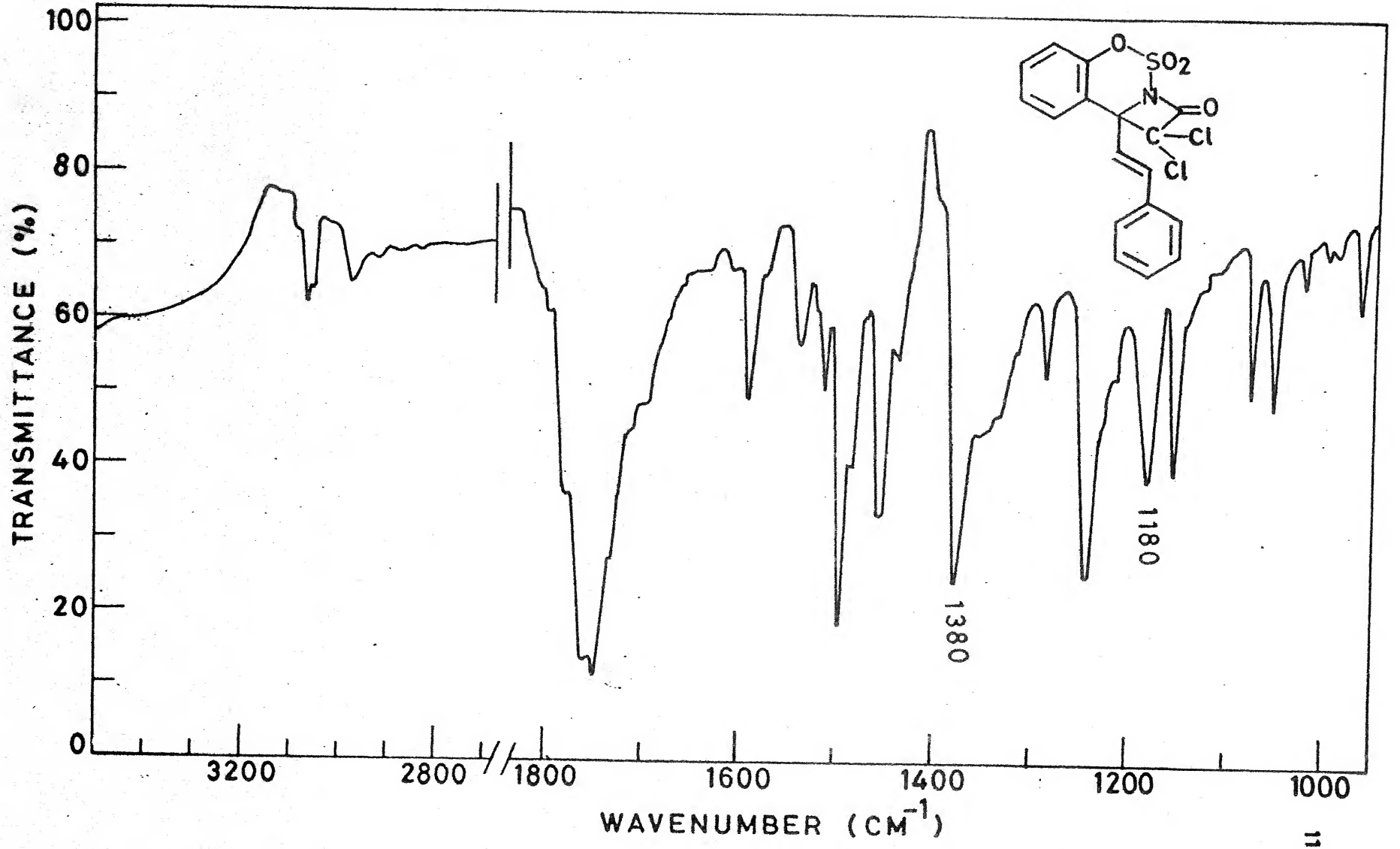


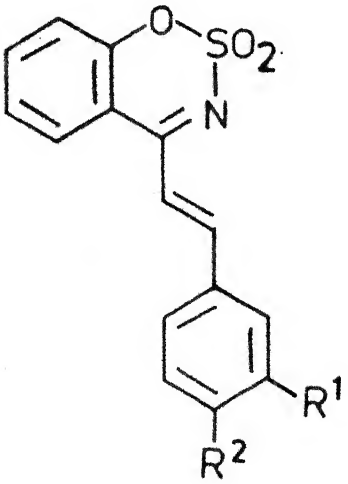
1 a - f + 7 → 10 a - f ; 10 g

in step (b-c), arises due to traces of moisture present in acetonitrile used as the solvent.

1-Morpholino-1-cyclohexene, 1-pyrrolidino-1-cyclopentene, and 1-piperidino-1-cyclopentene, react slowly with 1(a-f) to give the (4+2) cycloadducts 9, 10, 11 (a-f). Stirring the enamines with 1(a-f) for 48 hours at room temperature furnishes the products in 50-60% yield. These were purified by column chromatography over silica gel using benzene:ethylacetate (1:1) as an eluant. Changing the solvent from acetonitrile to dichloromethane or tetrahydrofuran did not substantially alter the yields of the products. Structure (10b) was established on the basis of IR, PMR and mass spectral data. The IR spectrum shows bands at 1380 and 1180 cm^{-1}, this indicates the presence of SO_2 group in the molecule. In the PMR spectrum eleven protons (methylene and methine) appear as a multiplet at δ 1.2-2.1. The benzyl proton and the four methylene protons of pyrrolidine ring (linked to nitrogen) show up as a multiplet at δ3.6. The olefinic and the aromatic protons appear as a complex multiplet at δ6.8-7.5. The mass spectrum of (10b) shows retro-Diels Alder fragmentation peak at m/z 456, 319 and 137. In the regio-isomer (10g) Hc should have appeared at δ3.6 in the PMR spectrum. Thus the possibility of assigning structure (10g) for the adduct was ruled out.

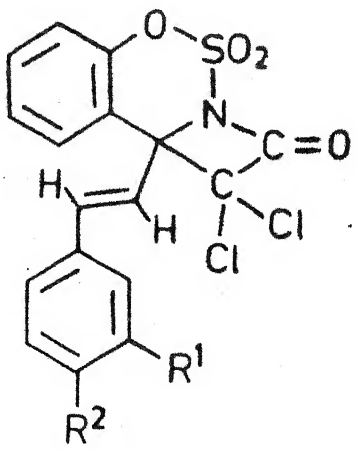

O
SO2
N
C=O
C
Cl
Cl
AROMATIC
TMS
9.0
8.0
7.0
0
PPM (δ)


100
80
60
40
20
0
TRANSMITTANCE (%)
3200
2800
1800
1600
1400
1200
1000
WAVENUMBER (CM⁻¹)
1380
1180
O
SO2
N
O
C
Cl
Cl



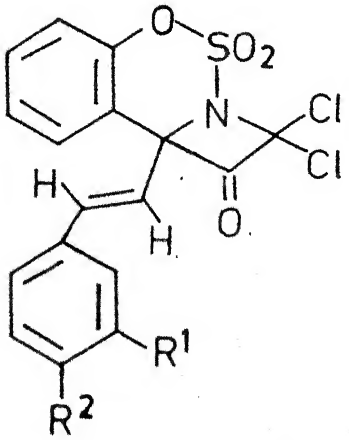
+ $Cl_2C{=}C{=}O$ ⟶

6

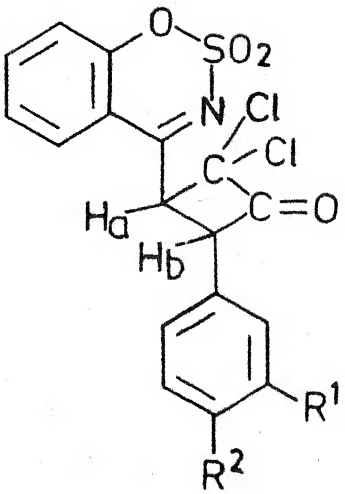


1 a - f

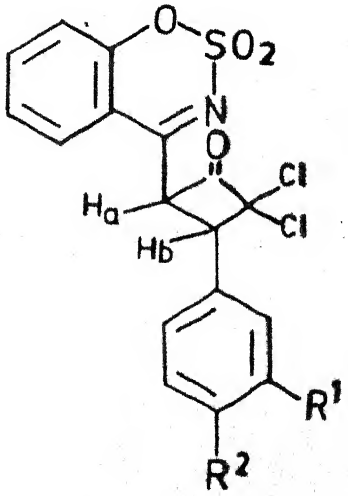
12 a



12 b



12 c



12 d

Reaction with dichloroketene:

Dichloro ketene, generated *in situ* from dichloroacetyl chloride and triethylamine, reacts slowly with 1a in refluxing dichloromethane to furnish (12a) in 20% yield. The IR spectrum shows absorption bands at 1380 and 1180 cm^{-1}, which indicates the presence of SO_2 group in the molecule. The absorption band due to C=N group was found to be conspicuously absent. The strong absorption band located at 1750 cm^{-1} in the IR spectrum confirms the presence of a carbonyl group. The PMR spectrum shows only a complex multiplet in the aromatic region. The alternate structures (12b, 12c and 12d) have been ruled out on the basis of spectral (IR & NMR) evidences. Thus, the formation of (12b) would arise by the addition of dichloroketene across the C=N, in a direction opposite to that postulated for (12a). On the other hand if the addition of dichloroketene had taken place at the olefinic centre, it would lead to the possibility of formation of two regio-isomers (12c and 12d). All these compounds would normally show $\nu_{C=O}$ at around 1800 cm^{-1}. Structures (12c) and (12d) would be expected to show $\nu_{C=N}$ at around 1620 cm^{-1}. Whereas, the compound, prepared by us, was characterized by the carbonyl absorption at 1750 cm^{-1}. Furthermore, there is a conspicuous absence of the AB quartet in the spectra of the compound. Both these evidences favour structure (12a) in preference to the other structures described above.

Attempted Diels-Alder Reaction:

Various dienophiles (namely vinyl-acetate, ethyl-acrylate, methyl vinylketone, chalcone, N-phenyl maleimide, butyl vinyl ether, dimethyl acetylene dicarboxylate and nitrones) failed to react with 4-styryl-1,2,3-benzoxathiazine-2,2-dioxide, after prolonged heating (80-130^{o}) and even in the presence of a Lewis acid, $AlCl_3$.

EXPERIMENTAL

All the melting points are uncorrected and were determined on a Fischer Johns melting point apparatus. IR spectra were recorded on Perkin-Elmer model-580 infra red spectrophotometer. Proton magnetic resonance (PMR) spectra were recorded on Varian EM-390 (90 MHz) instrument. Mass-spectra were recorded on a Jeol JMS-300D mass spectrometer at 70 eV. The elemental analyses were carried out in Coleman automatic carbon, hydrogen and nitrogen analysers.

Preparation of 4-Styryl-1,2,3-benzoxathiazine-2,2-dioxides

To a stirred solution of the 2'-hydroxychalcone (0.046g) in toluene (40 ml) at 100-105^{o}C was added chlorosulfonyl isocyanate (2:4 ml, 0.046 mol) in toluene (5 ml) over a period of 20 minutes. Stirring was continued for 3h at this temperature. The toluene was distilled off *in vacuo* and the residue was added to cold water

(50 ml). The solid was filtered, washed with water and recrystallized from ethanol to yield the various desired 4-styryl-1,2,3-benzoxathiazine-2,2-dioxides.

Reaction of 4-styryl-1,2,3-benzoxathiazine-2,2-dioxides (SBD) with 1-pyrrolidino-1-cyclohexene and 1-piperidino-1-cyclohexene (General Procedure):

Enamine (0.001 mol) was added to a magnetically stirred solution of 1(a-f) (0.285g, 0.001 mol) in dry acetonitrile (5 ml). The reaction products separated out immediately as pure crystalline solids, which were collected by filtration. The yields and the melting points of the products obtained are collected in Table .

Enamines	SBD in (g)	Product Yield(%)	M.P.(^{o}C)
1	2	3	4
1	0.285	98	140
2	0.319	97	157
3	0.364	93	167
4	0.299	91	145
5	0.315	98	180
6	0.346	97	172
7	0.284	99	160

...contd..

1	2	3	4
8	0.320	93	167
9	0.364	92	169
10	0.300	97	175
11	0.315	98	170
12	0.347	95	145

Reaction of 1(a-f) with 1-Morpholino-1-cyclohexene, 1-Pyrrolidino-1-cyclopentene and 1 Piperidino-1-cyclopentene (General Procedure):

To a stirred solution of 1 (a-f) (0.001 mol) in dry acetonitrile (5 ml), 6, 7, 8(a-f) (0.001 mol) was added at room temperature ($\sim 20^{\circ}$). The stirring was continued for 48 h. The solvent was removed under diminished pressure. The residue on silica gel column chromatography, using ethyl acetate:benzene mixture (1:1) as a eluent, yielded the pure 9, 10, 11(a-f).

Reaction of dichloroketene with 1 :

Dichloroacetyl chloride (0.147g, 0.001 mol), was added to a stirred solution of (1a) (0.285g, 0.001 mol) in dry dichloromethane (10 ml). This was followed by the addition of dry triethyl amine (2 ml). The reaction mixture was refluxed under nitrogen atmosphere for 6 h. Water (10 ml) was added to the

reaction mixture and organic layer was separated. It was washed with water, dried ($MgSO_4$) and the solvent was removed under diminished pressure. The residue on silica gel column chromatography, using benzene as a eluent, furnished pure (12a), as an oil (0.079g, 20%).

Synthesis of (4a)	:	Yield: 0.405g (98%), m.p. 140°.
Calcd for $C_{27}H_{30}N_2O_2$	:	C: 78.76; H: 7.24; N: 6.76
Found	:	C: 78.72; H: 7.29; N: 6.70%
IR spectrum (KBr) ν_{max}	:	3100, 2990, 1670 (ν_{CO}) cm^{-1}.
PMR spectrum (DMSO d_6), δ ppm	:	1.7 (m, 12H), 2.8 (s, 3H, CH_3), 3.8 (m, 5H), 6.7 (d, 1H), 7.2 (m, 9H).
Mass spectrum	:	m/z: 414(M^+), 413(M^+-1).
Synthesis of (4b)	:	Yield: 0.434g (97%), m.p.157°.
Calcd for $C_{27}H_{29}ClN_2O_2$	:	C: 72.24; H: 6.46; N: 6.24
Found	:	C: 72.27; H: 6.41; N: 6.19%
IR spectrum (KBr) ν_{max}	:	3120, 2990, 1665 (ν_{CO}) cm^{-1}.
PMR spectrum (DMSO d_6), δppm	:	1.6 (m, 12H), 2.7 (s, 3H, CH_3), 3.8 (m, 5H), 6.75 (d, 1H), 7.3 (m, 8H).
Mass spectrum	:	m/z: 448 (M^+).

Synthesis of (4c) : Yield: 0.458g (93%), m.p.167°.

Calcd for $C_{27}H_{29}BrN_2O_2$: C: 65.72; H: 5.88; N: 5.67

Found : C: 65.69; H: 5.81; N: 5.63%

IR spectrum (KBr)ν_{max} : 3100, 2995, 1680 (ν_{CO}) cm^{-1}.

PMR spectrum (DMSO-d_6), δ ppm : 1.65 (m, 12H), 2.65 (s, 3H, CH_3), 3.8 (m, 5H), 6.7 (d, 1H), 7.3 (m, 8H).

Mass spectrum : m/z: 493 (M^+).

Synthesis of (4d) : Yield: 0.389g (91%), m.p.145°.

Calcd for $C_{28}H_{32}N_2O_2$: C: 78.50; H: 7.47; N: 6.54

Found : C: 78.42; H: 7.35; N: 6.63%

IR spectrum (KBr)ν_{max} : 3100, 2995, 1675 (ν_{CO}) cm^{-1}.

PMR spectrum (DMSO-d_6), δ ppm : 1.65 (m, 12H), 2.3 (s, 3H, CH_3), 2.65 (s, 3H, CH_3), 3.8 (m, 5H), 6.65 (d, 1H), 7.4 (m, 8H).

Mass spectrum : m/z: 428 (M^+).

Synthesis of (4e) : 0.435g (98%), m.p. 180°.

Calcd for $C_{28}H_{32}N_2O_3$: C: 75.67; H: 7.20; N: 6.30

Found : C: 75.71; H: 7.11; N: 6.36%

IR spectrum (KBr)ν_{max} : 3100, 2980, 1680 (ν_{CO}) cm^{-1}.

PMR spectrum (DMSO-d_6), δ ppm : 1.7 (m, 12H), 2.65 (s, 3H, CH_3), 3.7 (s, 3H, OCH_3), 3.8 (m, 5H), 6.65 (d, 1H), 7.5 (m, 8H).

Mass spectrum : m/z: 444 (M^+).

Synthesis of (4f) : Yield: 0.459g (97%), m.p. 172°.

Calcd for $C_{29}H_{34}N_2O_4$: C: 73.41; H: 7.17; N: 5.90

Found : C: 73.36; H: 7.10; N: 5.83%

IR spectrum (KBr) ν_{max} : 3100, 2980, 1670 (ν_{CO}) cm^{-1}.

PMR spectrum (DMSO-d_6), δ ppm : 1.7 (m, 12H), 2.7 (s, 3H, CH_3), 3.7 (s, 6H, OCH_3), 3.8 (m, 5H), 6.7 (d, 1H), 7.4 (m, 7H).

Mass spectrum : m/z: 474 (M^+).

Synthesis of (5a) : Yield: 0.423g (99%), m.p. 160°.

Calcd for $C_{28}H_{32}N_2O_2$: C: 78.50; H: 7.47; N: 6.54

Found : C: 78.39; H: 7.56; N: 6.41%

IR spectrum (KBr) ν_{max} : 3080, 2940, 1650 (ν_{CO}) cm^{-1}.

PMR spectrum (DMSO-d_6), δ ppm : 1.5-1.9 (m, 14H), 2.8 (s, 3H, CH_3), 3.8 (m, 5H), 6.7 (d, 1H), 7.2 (m, 9H).

Mass spectrum : m/z: 428 (M^+).

Synthesis of (5b) : Yield: 0.429g (93%), m.p. 167°.

Calcd for $C_{28}H_{31}ClN_2O_2$: C: 72.64; H: 6.70; N: 6.05

Found : C: 72.58; H: 6.53; N: 5.91%

IR spectrum (KBr) ν_{max} : 3075, 2935, 1655 (ν_{CO}) cm^{-1}.

PMR spectrum (DMSO-d_6), δ ppm : 1.5-1.9 (m, 14H), 2.8 (s, 3H, CH_3), 3.8 (m, 5H), 6.7 (d, 1H), 7.4 (m, 8H).

Mass spectrum : m/z: 462 (M^+).

Synthesis of (5c) : Yield: 0.466g (92%), m.p. 169°.

Calcd for $C_{28}H_{31}BrN_2O_2$: C: 66.27; H: 6.11; N: 5.52

Found : C: 66.19; H: 5.94; N: 5.48%

IR spectrum (KBr) ν_{max} : 3080, 2940, 1660 (ν_{CO}) cm^{-1}.

PMR spectrum (DMSO-d_6), δ ppm : 1.5-1.9 (m, 14H), 2.8 (s, 3H, CH_3), 3.8 (m, 5H), 6.7 (d, 1H), 7.5 (m, 8H).

Mass spectrum : m/z: 507 (M^+).

Synthesis of (5d) : Yield: 0.428g (97%), m.p. 175°.

Calcd for $C_{29}H_{34}N_2O_2$: C: 78.73; H: 7.69; N: 6.33

Found : C: 78.66; H: 7.82; N: 6.19%

IR spectrum (KBr) ν_{max} : 3085, 2950, 1665 (ν_{CO}) cm^{-1}.

PMR spectrum (DMSO-d_6), δppm : 1.5-1.9 (m, 14H), 2.8 (s, 3H, CH_3), 2.3 (s, 3H, CH_3), 3.8 (m, 5H), 6.7 (d, 1H), 7.5 (m, 8H).

Mass spectrum : m/z: 442 (M^+).

Synthesis of (5e) : Yield: 0.448g (98%), m.p. 170°.

Calcd for $C_{29}H_{34}N_2O_3$: C: 75.98; H: 7.42; N: 6.11

Found : C: 75.82; H: 7.23; N: 6.02%

IR spectrum (KBr) ν_{max} : 3080, 2945, 1670 (ν_{CO}) cm^{-1}.

PMR spectrum (DMSO-d_6), δ ppm : 1.5-1.9 (m, 14H), 2.8 (s, 3H, CH_3), 3.8 (m, 5H), 3.7 (s, 3H, OCH_3), 6.7 (d, 1H), 7.4 (m, 8H).

Mass spectrum : m/z: 458 (M^+).

Synthesis of (5f) : Yield: 0.463g (95%), m.p. 145°.

Calcd for $C_{30}H_{36}N_2O_4$: C: 73.77; H: 7.37; N: 5.73

Found : C: 73.63; H: 7.42; N: 5.90%

IR spectrum (KBr) ν_{max} : 3085, 2930, 1670 (ν_{CO}) cm^{-1}.

PMR spectrum (DMSO-d_6), δ ppm : 1.5-1.9 (m, 14H), 2.8 (s, 3H, CH_3), 3.8 (m, 5H), 3.7 (s, 6H, OCH_3), 6.7 (d, 1H), 7.5 (m, 7H).

Mass spectrum : m/z: 488 (M^+).

Synthesis of (9a) : Yield: 0.151g (53%), m.p. 168°.

Calcd for $C_{25}H_{28}N_2O_4S$: C: 66.37; H: 6.19; N: 6.19

Found : C: 66.21; H: 6.03; N: 6.26%

IR spectrum (KBr) ν_{max} : 3080, 2910, 2970, 1380, 1180 (ν_{SO_2}) cm^{-1}.

PMR spectrum ($CDCl_3$), δppm : 1.2-2.1 (m, 9H), 3.6 (m, 9H), 6.8-7.5 (m, 9H, aromatic + 1H olefinic).

Mass spectrum : m/z: 285, 221, 167.

Synthesis of (9b) : Yield: 0.175g (55%), m.p. 171°.

Calcd for $C_{25}H_{27}ClN_2O_4S$: C: 61.66; H: 5.54; N: 5.75

Found : C: 61.52; H: 5.43; N: 5.63%

IR spectrum (KBr) ν_{max} : 3090, 2910, 2980, 1385, 1190 (ν_{SO_2}) cm^{-1}.

PMR spectrum ($CDCl_3$), δppm : 1.2-2.1 (m, 9H), 3.6 (m, 9H), 6.8-7.5 (m, 8H aromatic + 1H olefinic).

Mass spectrum : m/z: 319, 255, 167.

Synthesis of (9c) : Yield: 0.182g (50%), m.p. 160°.

Calcd for $C_{25}H_{27}BrN_2O_4S$: C: 56.49; H: 5.08; N: 5.27

Found : C: 56.31; H: 5.17; N: 5.10%

IR spectrum (KBr) ν_{max} : 3085, 2900, 2970, 1380, 1185 (ν_{SO_2}) cm^{-1}.

PMR spectrum ($CDCl_3$), δ ppm : 1.2-2.2 (m, 9H), 3.6 (m, 9H), 6.9-7.6 (m, 8H aromatic + 1H olefinic).

Mass spectrum : m/z: 364, 300, 167.

Synthesis of (9d) : Yield: 0.170g (51%), m.p. 160°.

Calcd for $C_{26}H_{30}N_2O_4S$: C: 66.95; H: 6.43; N: 6.00

Found : C: 66.81; H: 6.50; N: 6.09%

IR spectrum (KBr) ν_{max} : 3080, 2910, 2970, 1380, 1185 (ν_{SO_2}) cm^{-1}.

PMR spectrum ($CDCl_3$), δ ppm : 1.1-2.2 (m, 9H), 2.4 (s, 3H, CH_3), 3.6 (m, 9H), 6.9-7.6 (m, 8H aromatic + 1H olefinic).

Mass spectrum : m/z: 299, 255, 167.

Synthesis of (9e) : Yield: 0.152g (59%), m.p. 166°.

Calcd for $C_{26}H_{30}N_2O_5S$: C: 64.73; H: 6.22; N: 5.80

Found : C: 64.68; H: 6.12; N: 5.91%

IR spectrum (KBr) ν_{max} : 3080, 2910, 2970, 1390, 1180 (ν_{SO_2}) cm^{-1}.

PMR spectrum ($CDCl_3$), δ ppm : 1.1-2.2 (m, 9H), 3.6 (m, 12H), 6.8-7.5 (m, 8H aromatic + 1H olefinic).

Mass spectrum : m/z: 315, 251, 167.

Synthesis of (9f) : Yield: 0.192g (58%), m.p. 145°.

Calcd for $C_{27}H_{32}N_2O_6S$: C: 63.28; H: 6.25; N: 5.46

Found : C: 63.39; H: 6.15; N: 5.58%

IR spectrum (KBr) ν_{max} : 3085, 2910, 2970, 1375, 1185 (ν_{SO_2}) cm^{-1}.

PMR spectrum ($CDCl_3$), δ ppm : 1.1-2.2 (m, 9H), 3.5 (m, 15H), 6.8-7.5 (m, 7H aromatic + 1H olefinic).

Mass spectrum : m/z: 345, 281, 137.

Synthesis of (10a) : Yield: 0.165g (58%), m.p. 145°.

Calcd for $C_{24}H_{26}N_2O_3S$: C: 68.24; H: 6.16; N: 6.63

Found : C: 68.13; H: 6.03; N: 6.71%

IR spectrum (KBr) ν_{max} : 3080, 2910, 2970, 1380, 1180 (ν_{SO_2}) cm^{-1}.

PMR spectrum ($CDCl_3$), δ ppm : 1.1-2.1 (m, 11H), 3.6 (m, 5H), 6.6-7.4 (m, 9H aromatic + 1H olefinic).

Mass spectrum : m/z: 285, 221, 166, 137, 115.

Synthesis of (10b) : Yield: 0.165g (52%), m.p. 162°.

Calcd for $C_{24}H_{25}ClN_2O_3S$: C: 63.08; H: 5.47; N: 6.13

Found : C: 63.21; H: 5.33; N: 6.02%

IR spectrum (KBr) ν_{max} : 3080, 2910, 2970, 1380, 1180 (ν_{SO_2}) cm^{-1}.

PMR spectrum ($CDCl_3$), δppm : 1.2-2.1 (m, 11H), 3.6 (m, 5H), 6.6-7.5 (m, 8H aromatic + 1H olefinic).

Mass spectrum : m/z: 456, 319, 170, 255, 150, 112, 119, 137.

Synthesis of (10c) : Yield: 0.214g (59%), m.p. 155°.

Calcd for $C_{24}H_{25}BrN_2O_3S$: C: 57.43; H: 4.99; N: 5.58

Found : C: 57.56; H: 4.81; N: 5.63%

IR spectrum (KBr) ν_{max} : 3085, 2900, 2970, 1380, 1185 (ν_{SO_2}) cm^{-1}.

PMR spectrum ($CDCl_3$), δppm : 1.1-2.2 (m, 11H), 3.6 (m, 5H), 6.8-7.7 (m, 8H aromatic + 1H olefinic).

Mass spectrum : m/z: 364, 300, 195, 166, 157, 137.

Synthesis of (10d) : Yield: 0.164g (55%), m.p. 180°.

Calcd for $C_{25}H_{28}N_2O_3S$: C: 68.80; H: 6.42; N: 6.42

Found : C: 68.14; H: 6.23; N: 6.31%

IR spectrum (KBr) ν_{max} : 3080, 2910, 2970, 1380, 1185 (ν_{SO_2}) cm^{-1}.

PMR spectrum ($CDCl_3$), δ ppm : 1.1-2.2 (m, 11H), 2.4 (s, 3H, CH_3) 3.6 (m, 5H), 6.9-7.8 (m, 8H aromatic + 1H olefinic).

Mass spectrum : m/z: 299, 235, 166, 151, 137.

Synthesis of (10e) : Yield: 0.166g (53%), m.p. 171°.

Calcd for $C_{25}H_{28}N_2O_4S$: C: 66.37; H: 6.19; N: 6.19

Found : C: 66.22; H: 6.28; N: 6.37%

IR spectrum (KBr) ν_{max} : 3080, 2910, 2970, 1390, 1180 (ν_{SO_2}) cm^{-1}.

PMR spectrum ($CDCl_3$), δppm : 1.0-2.0 (11H), 3.6 (m, 5H), 3.8 (s, 3H, OCH_3), 6.8-7.5 (m, 8H aromatic + 1H olefinic).

Mass spectrum : m/z: 315, 251, 137.

Synthesis of (10f) : Yield: 0.203g (59%), m.p. 182°.

Calcd for $C_{26}H_{30}N_2O_5S$: C: 64.73; H: 6.22; N: 5.80

Found : C: 64.61; H: 6.13; N: 5.92%

IR spectrum (KBr) ν_{max} : 3085, 2910, 2970, 1375, 1185 (ν_{SO_2}) cm^{-1}.

PMR spectrum ($CDCl_3$), δ ppm : 1.2-2.2 (m, 11H), 3.5 (m, 5H), 3.8 (s, 6H, OCH_3), 6.7-7.5 (m, 7H aromatic + 1H olefinic).

Mass spectrum : m/z: 345, 281, 137.

Synthesis of (11a) : Yield: 0.142g (50%), m.p. 175°.

Calcd for $C_{25}H_{28}N_2O_3S$: C: 68.80; H: 6.42; N: 6.92

Found : C: 68.13; H: 6.51; N: 6.83%

IR spectrum (KBr) ν_{max} : 3080, 2910, 2980, 1385, 1190 (ν_{SO_2}) cm^{-1}.

PMR spectrum ($CDCl_3$), δ ppm : 1.2-2.2 (m, 13H), 3.6 (m, 5H), 6.8-7.5 (m, 9H aromatic + 1H olefinic).

Mass spectrum : m/z: 285, 221, 149.

Synthesis of (11b) : Yield: 0.175g (55%), m.p. 165°.

Calcd for $C_{25}H_{27}ClN_2O_3S$: C: 64.03; H: 5.76; N: 5.97

Found : C: 64.12; H: 5.61; N: 6.11%

IR spectrum (KBr) ν_{max} : 3080, 2900, 2980, 1370, 1180 (ν_{SO_2}) cm^{-1}.

PMR spectrum ($CDCl_3$), δ ppm : 1.2-2.3 (m, 13H), 3.6 (m, 5H), 6.6-7.5 (m, 8H aromatic + 1H olefinic).

Mass spectrum : m/z: 319, 166, 149.

Synthesis of (11c) : Yield: 0.189g (52%), m.p. 150°.

Calcd for $C_{25}H_{27}BrN_2O_3S$: C: 58.47; H: 5.26; N: 5.45

Found : C: 58.31; H: 5.42; N: 5.37%

IR spectrum (KBr) ν_{max} : 3085, 2900, 2970, 1380, 1185 (ν_{SO_2}) cm^{-1}.

PMR spectrum ($CDCl_3$), δ ppm : 1.1-2.2 (m, 13H), 3.6 (m, 5H), 6.7-7.5 (m, 8H aromatic + 1H olefinic).

Mass spectrum : m/z: 364, 300, 149.

Synthesis of (11d) : Yield: 0.161g (54%), m.p. 161°.

Calcd for $C_{26}H_{30}N_2O_3S$: C: 69.64; H: 6.69; N: 6.25

Found : C: 69.51; H: 6.80; N: 6.43%

IR spectrum (KBr) ν_{max} : 3080, 2910, 2970, 1385, 1180 (ν_{SO_2}) cm^{-1}.

PMR spectrum ($CDCl_3$), δ ppm : 1.2-2.2 (m, 13H), 2.3 (s, 3H, CH_3), 3.6 (m, 5H), 6.9-7.8 (m, 8H aromatic + 1H olefinic).

Mass spectrum : m/z: 299, 235, 149.

Synthesis of (11e) : Yield: 0.166g (53%), m.p. 171°.

Calcd for $C_{26}H_{30}N_2O_4S$: C: 67.24; H: 6.46; N: 6.03

Found : C: 67.17; H: 6.21; N: 6.24%

IR spectrum (KBr) ν_{max} : 3080, 2910, 2970, 1390, 1180 (ν_{SO_2}) cm^{-1}.

PMR spectrum ($CDCl_3$), δ ppm : 1.2-2.2 (m, 13H), 3.6 (m, 5H), 3.8 (s, 3H, OCH_3), 6.8-7.5 (m, 8H aromatic + 1H olefinic).

Mass spectrum : m/z: 315, 251, 149.

Synthesis of (11f) : Yield: 0.172g (50%), m.p. 165°.

Calcd for $C_{27}H_{32}N_2O_5S$: C: 65.58; H: 6.47; N: 5.66

Found : C: 65.71; H: 6.39; N: 5.73%

IR spectrum (KBr) ν_{max} : 3085, 2910, 2975, 1375, 1185 (ν_{SO_2}) cm^{-1}.

PMR spectrum ($CDCl_3$), δ ppm : 1.2-2.2 (m, 13H), 3.6 (m, 5H), 3.8 (s, 6H, OCH_3), 6.7-7.5 (m, 7H aromatic + 1H olefinic).

Mass spectrum : m/z: 345, 281, 149.

Synthesis of (12a) : Yield: 0.079g (20%), oil.

Calcd for $C_{17}H_{11}Cl_2O_4NS$: C: 51.64; H: 2.78; N: 3.54

Found : C: 51.62; H: 2.89; N: 3.41%

IR spectrum (Neat) ν_{max} : 3080 (aromatic), 1750 ($\nu_{C=O}$), 1380, 1180 (ν_{SO_2}) cm^{-1}.

PMR spectrum ($CDCl_3$), δppm : 7.2-7.7 (m, 9H aromatic + 2H olefinic).

Mass spectrum : m/z: 395 (M^+).

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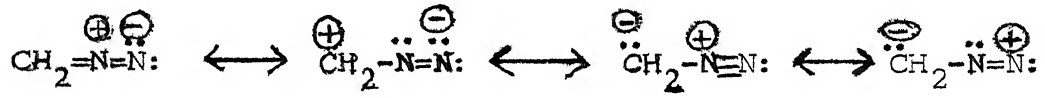
CHAPTER II-B

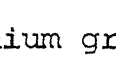
REACTION OF 4-STYRYL-1,2,3-BENZOXATHIAZINE-2,2-DIOXIDES WITH DIAZOMETHANE

Diazomethane is best represented as a resonance hybrid derived from linear resonating structures with opposing dipoles.



(i) (ii) (iii) (iv)

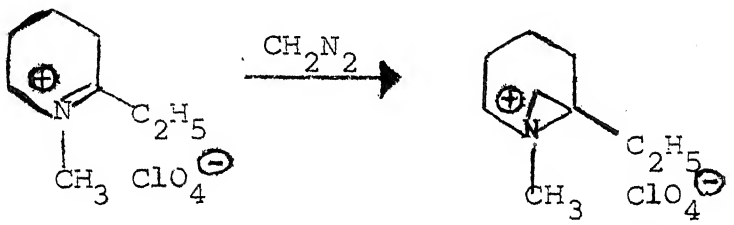
Under appropriate conditions diazomethane can behave either as an electrophile (ii) nucleophile, (iii) a 1,3 dipole or (iv) as a source of methylene.

Diazomethane can be added successfully to the ternary iminium grouping () contained in monocyclic, bicyclic and tricyclic systems. An aziridinium salt, such as 5-azoniadispiro (4.0.5.1) dodecane perchlorate (2,2-penta-methylene-1,1-tetra-methylene aziridinium perchlorate) can be made simply and in high yield by the nucleophilic attack of diazomethane on the corresponding ternary iminium perchlorate.

The endocyclic iminium system employed was 2-ethyl-1-methyl-Δ'-tetrahydropyridinium perchlorate ($C_8H_{16}ClNO_4$) (186) made via the mercuric acetate oxidation of 2-ethyl-1-methyl piperidine. When this compound, in methylene chloride, was treated with

diazomethane in ether at 0°, a new product 6-ethyl-1-methyl-1-azoniabicyclo [4.1.0]-heptane perchlorate (187) was formed (Scheme II. 55).

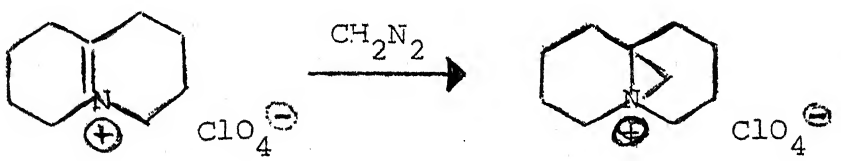
Scheme II.55



(186) (187)

In the bicyclic series, $\Delta^{5(10)}$ -dehydroquinolizidinium perchlorate (188 was converted to 1-azoniatricyclo [4.4.1.0] undecane perchlorate in 90% yield by treatment with diazomethane[2].

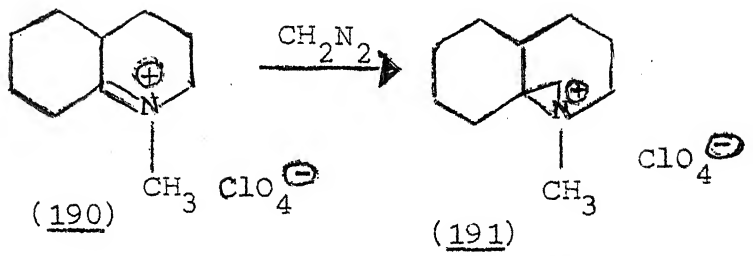
Scheme II.56



(188) (189)

Another bicyclic system investigated was 1-methyl-Δ'-octahydroquinolinium perchlorate. Reaction of the compound with diazomethane proceeded rapidly and in high yield.

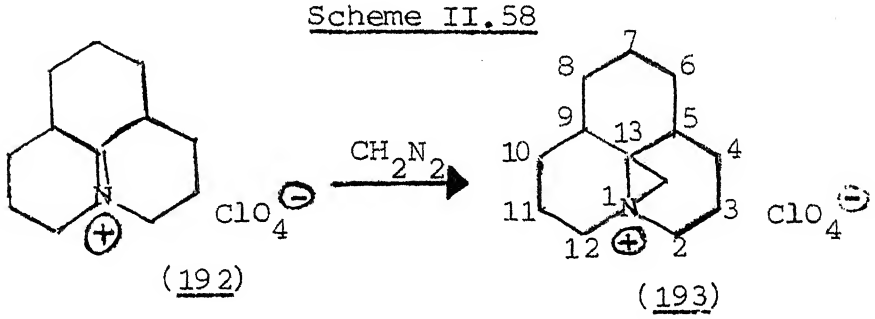
Scheme II.57



(190) (191)

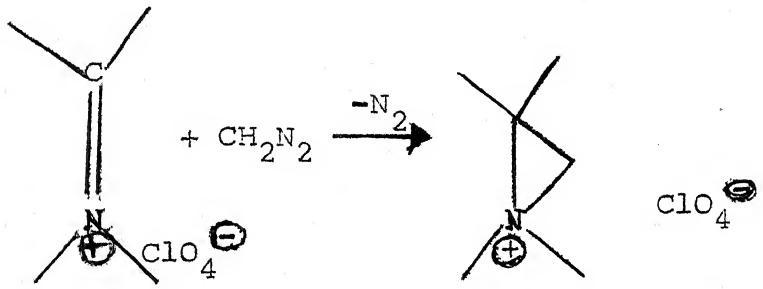
The reaction of diazomethane with >C=N< group in a tricycli system, is exemplified with Δ'-tetrahydrojulolidinium perchlorate.

Scheme II.58



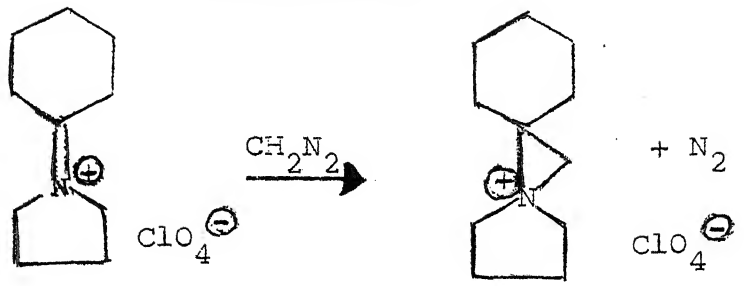
(192) (193)

Three membered ring formation occurs when diazomethane is allowed to react on certain C=S, C=O & C=N functions.[3]



N-Cyclohexylidene pyrrolidinium perchlorate (194) reacts rapidly with diazomethane in methanol-ether solution at -10° to give (195).[4]

Scheme II.59



(194) (195)

Alkane sulfonyl chlorides, when treated with diazomethane in the presence of a base (usually a tertiary amine) give sulfenes. The base removes hydrochloric acid from the sulfonyl halide to produce the highly reactive sulfene (197), which then adds to CH_2N_2. The episulfone (199) on heating produces the corresponding alkene (200).

Scheme II.60

$$RCH_2SO_2Cl \xrightarrow{R_3'N} [RCH{=}SO_2]$$

(196) (197)

$$[RCH{=}SO_2] + CH_2N_2 \longrightarrow R{-}CH(\text{--}SO_2\text{--}CH_2) \quad (199)$$

(198)

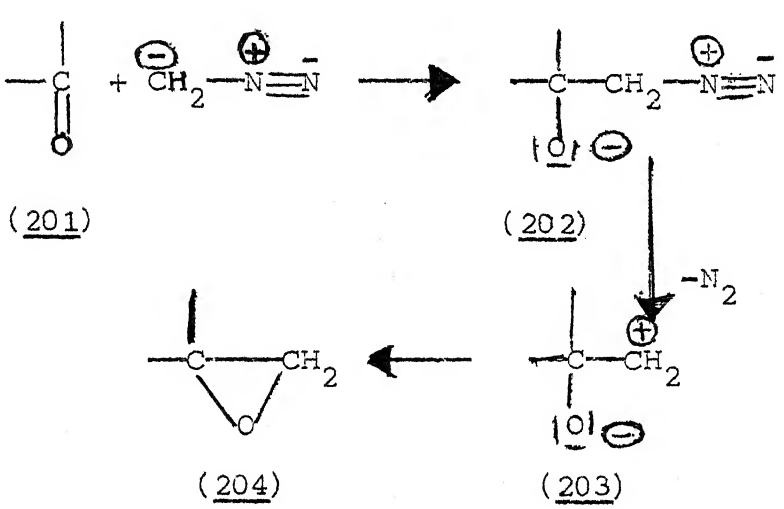
$$\downarrow \Delta$$

$$RCH{=}CH_2$$

(200)

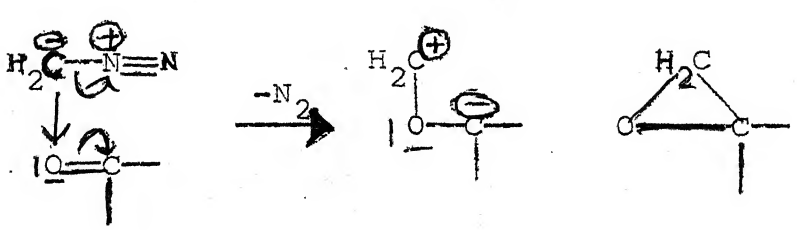
Aldehydes and ketones can also be converted to epoxides by treatment with diazomethane[3], but an important side reaction is the formation of an aldehyde or ketone with one more carbon than the starting compound. The reaction can be carried out with many aldehydes, ketones and quinones. The mechanism that accounts for the formation of the epoxide[8] is given in Scheme II.61 (vide infra).

Scheme II.61



(201) (202) (203) (204)

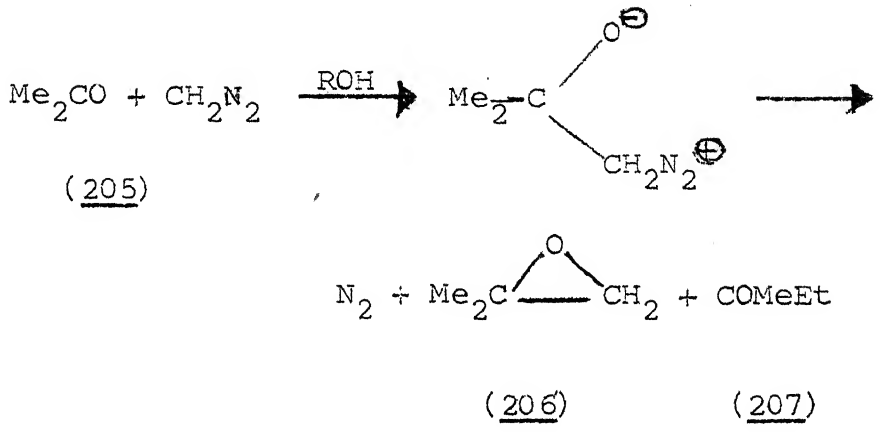
Scheme II.62



Diazomethane reacts rapidly with acetone in the presence of hydroxylic promoters to give a mixture of ethyl methyl ketone(207

and 1,2 epoxy-2-methyl propane (206), the reaction being usually represented as,

Scheme II.63

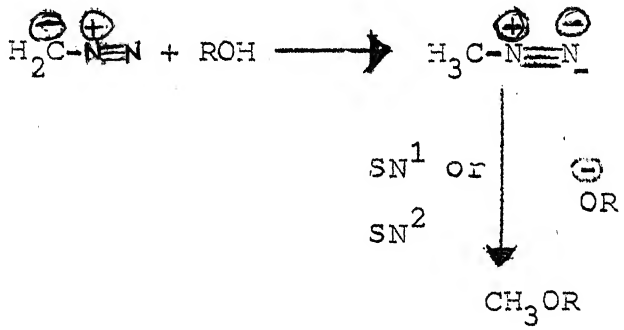


The reaction is normally carried out in an inert solvent, such as, di-ethyl ether and may take several days to reach completion. Use of Lewis acids e.g. BF_3 or $AlCl_3$ as catalyst, reduces reaction time considerably and yields predominantly the homologous ketone.

Diazomethane reacts with alcohols to produce methyl ethers. The reaction involves milder reaction conditions and the products are obtained in fairly high yields. This reaction is therefore useful in the methylation of alcohols and phenols, which are expensive and are available only in limited amounts.

$$CH_2N_2 + ROH \xrightarrow{HBF_4} CH_3OR$$

Hydroxy compounds react better as their acidity increase and ordinary alcohols do not react at all unless HBF_4[9] or $AlCl_3$[10] is present as a catalyst. The more acidic phenols react very wel in the absence of the catalyst.



Oximes and ketones which have substantial enolic contributions, give O-alkylation to form, respectively, O-alkyl oximes and enol ethers.

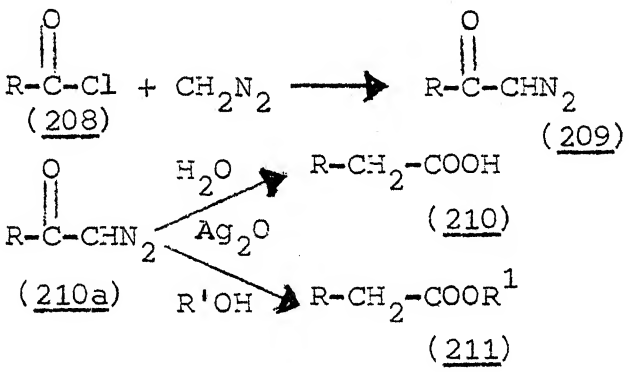
Diazomethane has been successfully employed in the alkylation of primary and secondary amines. Diaryl and aryl alkylamines are, however, reported to react very poorly. The acidity of amines is not great enough for the reaction to proceed without a catalyst, but BF_3, which converts the amine to the $F_3B\text{-}NHR'_2$, complex, enables the reaction to take place. CuCN is also used as a catalyst.[11]

$$CR_2N_2 + R'_2NH \xrightarrow{BF_3} CHR_2NR'_2$$

Acids can be converted to esters with diazo-compounds. In contrast to alcohols, carboxylic acids undergo the reaction quite well at room temperature, since the reactivity of the reagent increases with acidity. In this reaction high yields of products are obtained. It is often used where the acid is sensitive to higher temperatures.

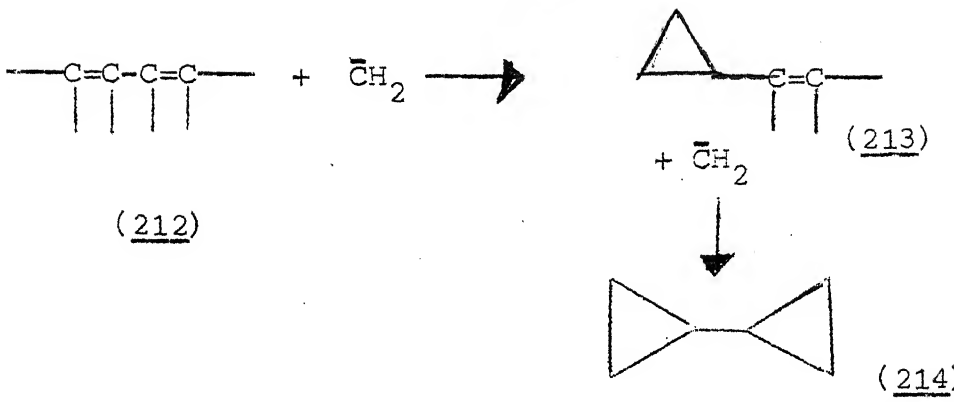
$$CH_2N_2 + RCOOH \longrightarrow RCOOCH_3$$

An acyl halide is (208) converted to (209) a carboxylic acid with one additional carbon atom.



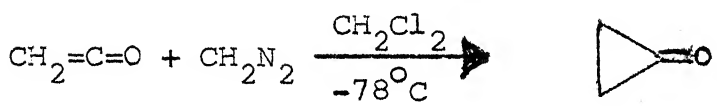
The actual rearrangement occurs in the second step of the reaction i.e., on treatment of the diazoketone with water and silver oxide or with silver benzoate and triethylamine. An ester RCH_2COOR^1 results if alcohol is substituted for water in the above reaction. Likewise, amide is produced when (210a) is reacted with ammonia. Olefines of all types can be converted to cyclopropane derivatives by addition of diazomethane. Conjugated dienes give 1,2-addition[12] (Scheme II.64) products.

Scheme II.64

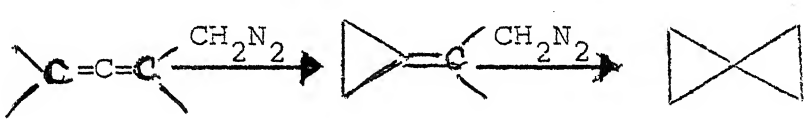


(212) (213) (214)

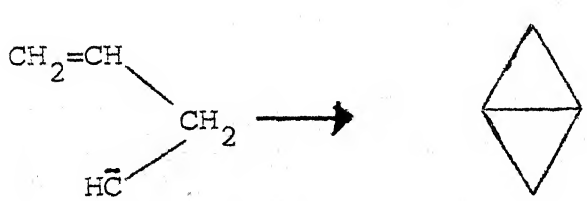
Diazomethane adds to ketene to give cyclopropanone.[13,14]



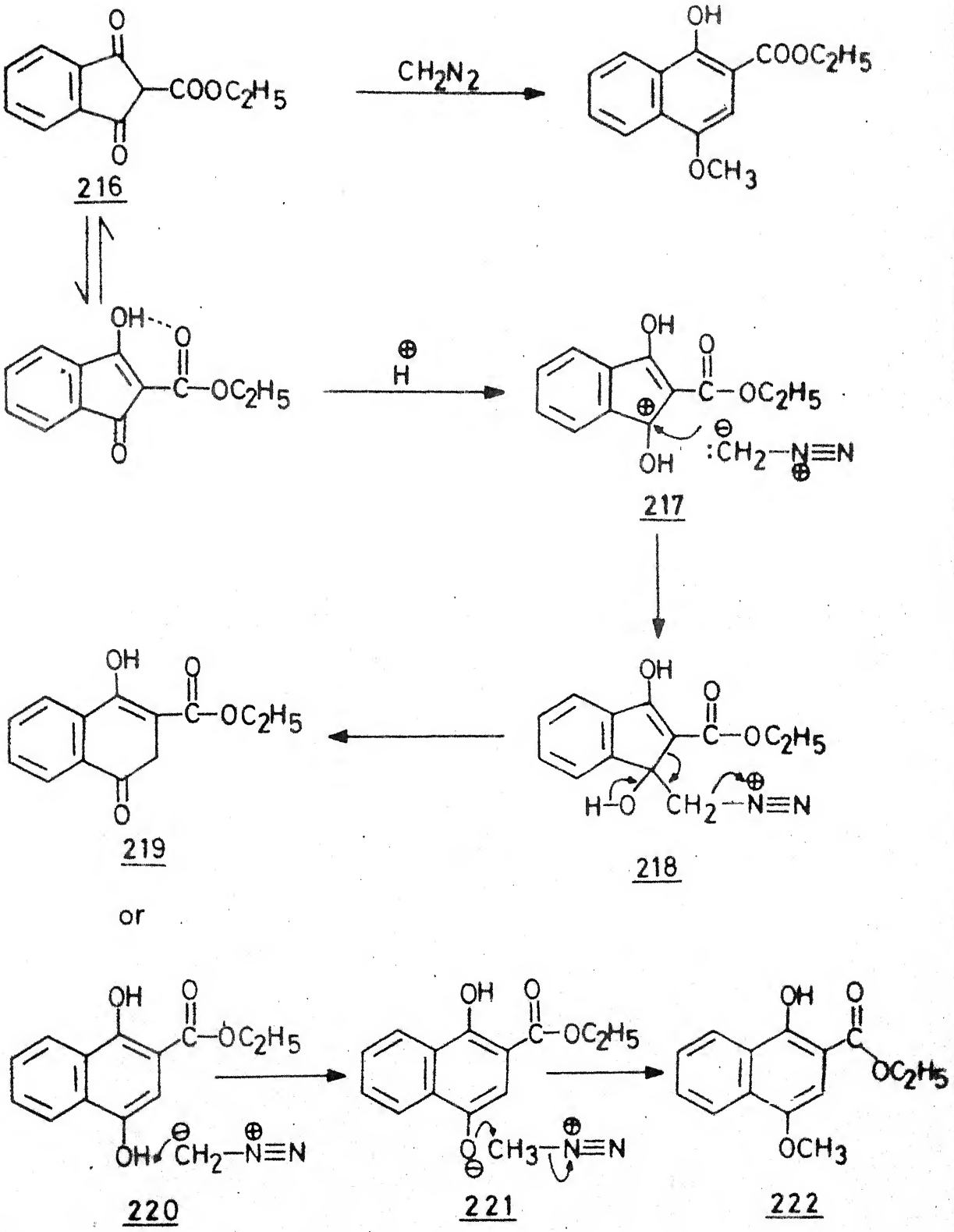
Allenes react with carbenes to give cyclopropanes with exocyclic unsaturation.[15] A second mole of CH_2N_2 gives spiro pentanes.



Allyl carbene gives internal addition, forming bicyclobutane.[16]

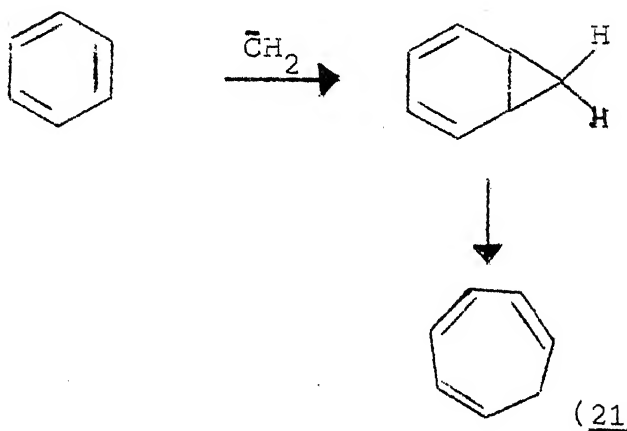


Scheme II.66


COOC2H5
CH2N2
OH
COOC2H5
OCH3
216
OH
C–OC2H5
H
:CH2–N≡N
217
H–O
CH2–N≡N
218
219
or
OH–CH2–N≡N
220
O–CH3–N≡N
221
222

The *in situ* generated methylene, from diazomethane and cuprous bromide, is reported[17] to react with benzene to produce tropilidene.(215).

Scheme II.65

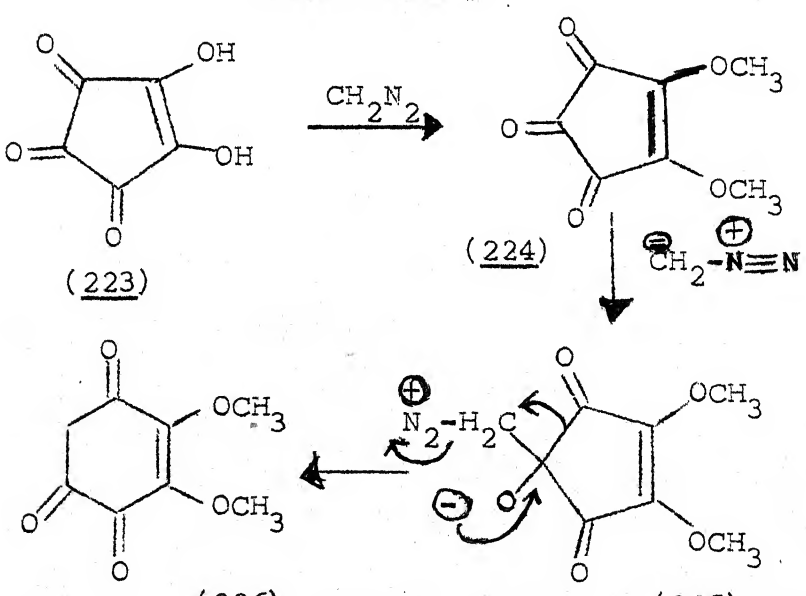


(215)

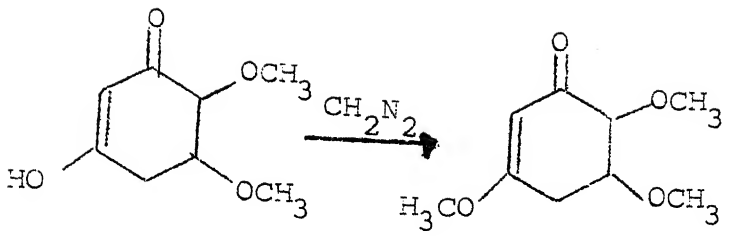
Rearrangement reactions take place with diazomethane to give ring expanded products[18] as shown in the Scheme II.66 .

Another example of rearrangement is as follows:-

Scheme II.67

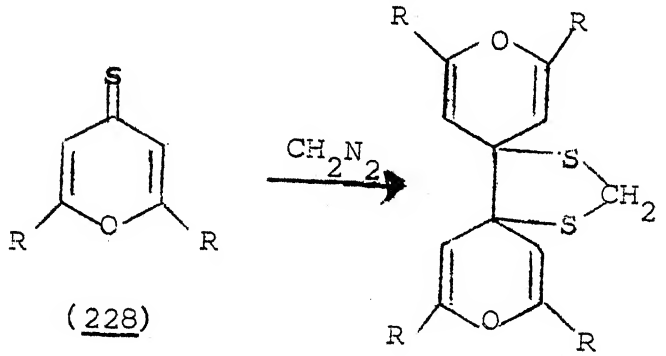


(223) (224) (226) (225)



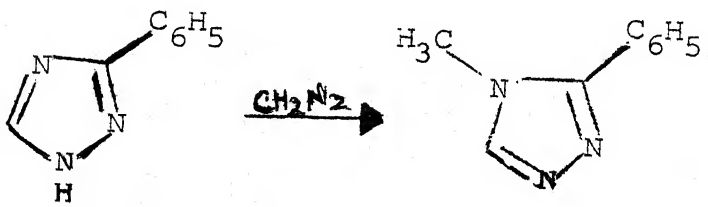
(227)

Unusual reactions occur between diazomethane and heterocyclic thiocarbonyl compounds. Pyran-4-thiones[22] give methylene ethers of 1,2-dimercaptans formed by dimerization of (228). 4-thioflavones[22,23] and 4-thiochromones[22,24] are reported to react similarly.



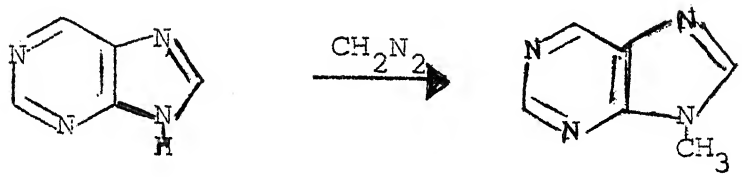
(228) (229)

3(5)-Phenyl-1,2,4-triazole (230) is converted into 1-methyl-5-phenyl-1,2,4-triazole (231)[25], by diazomethane.



(230) (231)

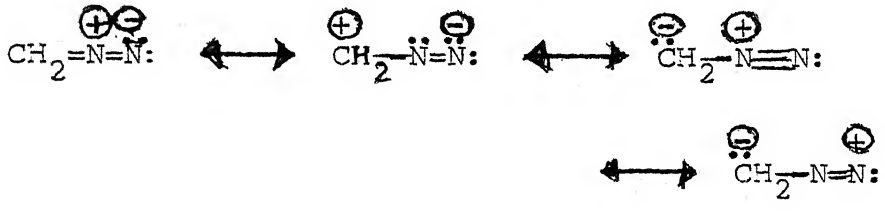
Purine reacts[26] with diazomethane to afford 9-methyl purine (233).



(232) (233)

RESULTS AND DISCUSSION

Diazomethane is best represented as a resonance hybrid derived from linear resonating structures with opposing dipoles:

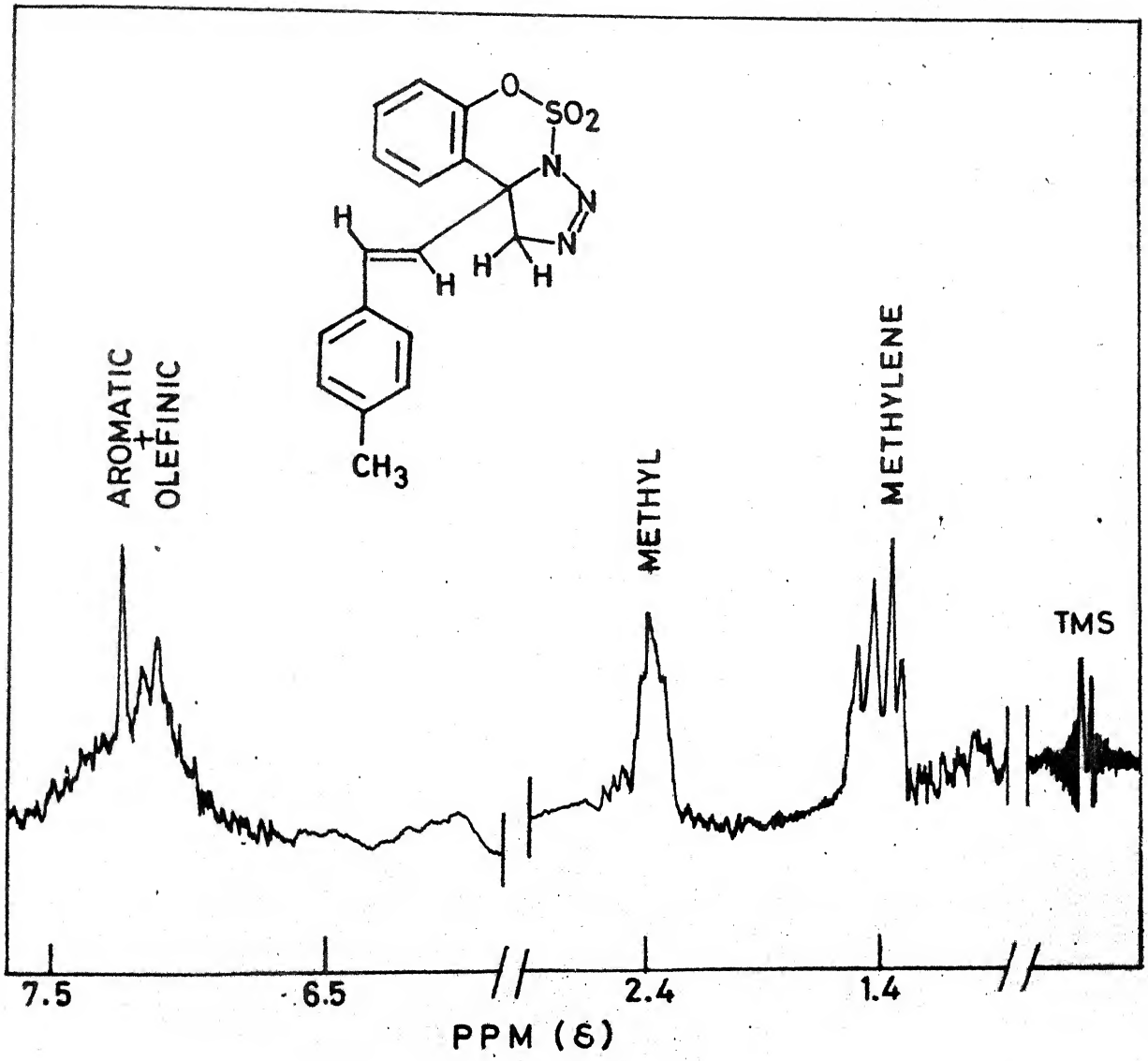


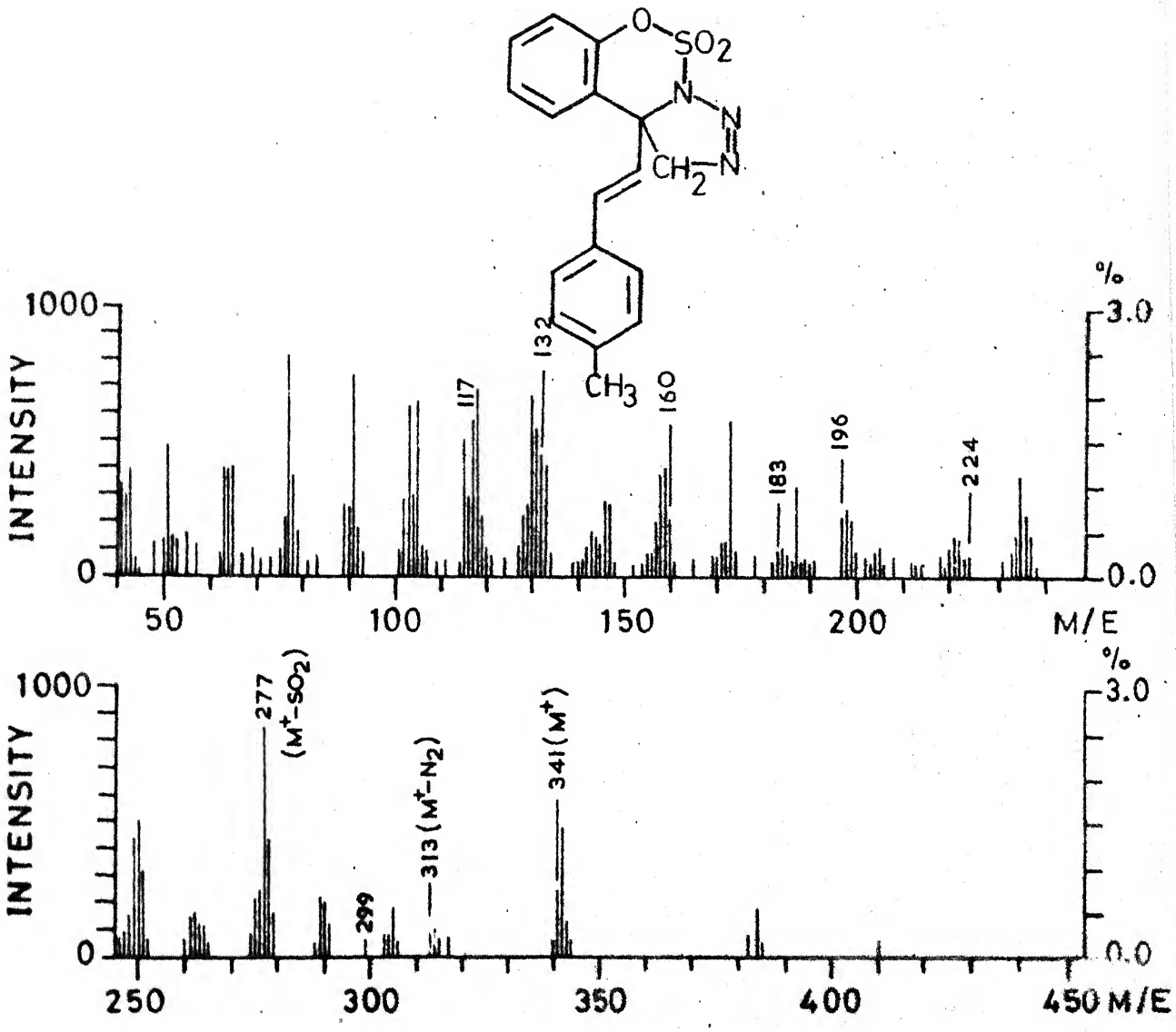
Under appropriate conditions, diazomethane can behave either as an (i) electrophile (ii) nucleophile (iii) a 1,3-dipole or (iv) as a source of methylene. The heterodiene (1a) contains C=C bond and C=N bond in conjugation. The diazomethane can undergo [3+2] addition across the C=C bond[20] or across the C=N bond.[21] Compounds (1a-f) undergo smooth reaction with diazomethane in dichloromethane-ether mixture at room temperature, to furnish (3a-f) in 76-82% yield. The reaction is fast and is completed within a

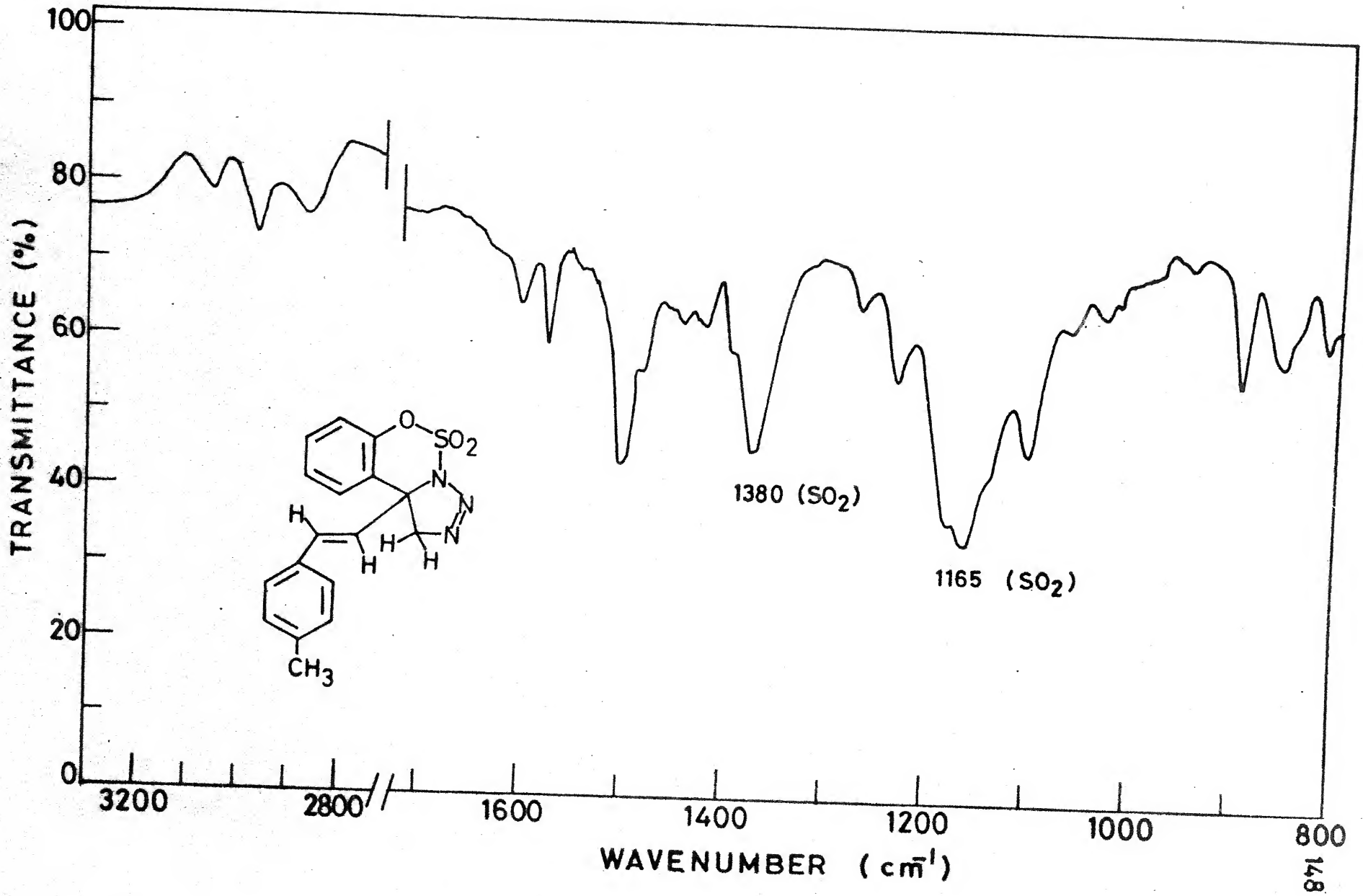
few minutes. The structure was assigned unequivocally on the basis of spectral data. The IR absorption maxima at 1380 and 1150 cm^{-1} indicates the presence of SO_2 group in the molecule. The mass fragmentation pattern clearly shows that only one molecule of diazomethane has been added up. The PMR spectrum shows a quartet at δ1.4 corresponding to two protons. The remaining protons show up as a complex multiplet in the aromatic region (δ7.0-7.6).The methylene protons should have come arou δ3. An examination of the Drieding model shows that the two methylene protons lie in the shielding cone of the double bond and hence appear upfield at δ1.4. Structure 4 is expected if the addition of diazomethane were to take place in the opposite direction.

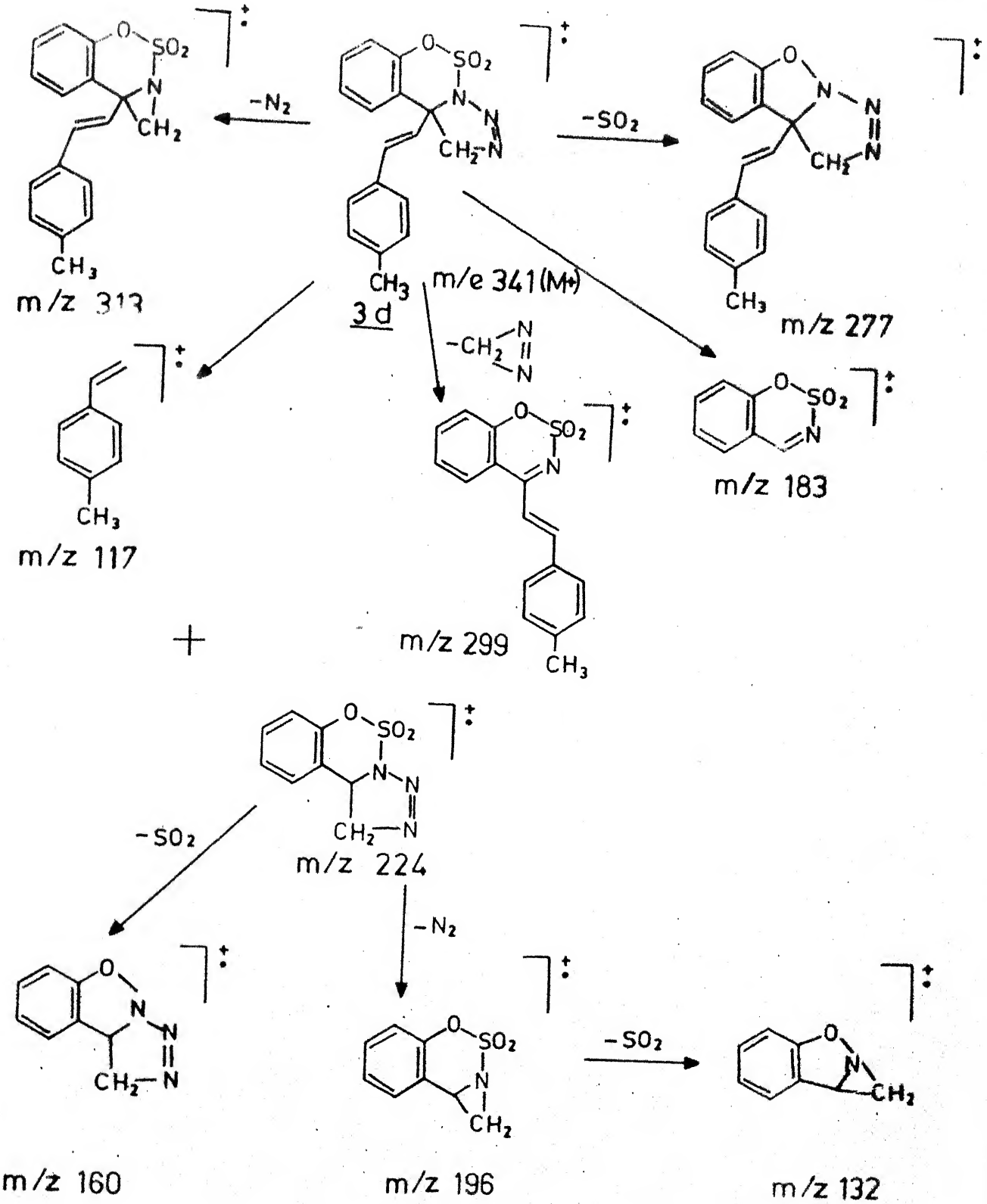
The PMR signal due to methylene protons sandwiched between two nitrogen atoms (vide structure 4) should appear relatively at lower field i.e. δ5. The signal is actually observed at δ 1.4 and this therefore, rules out the structure 4 for the cyclo-adduct.

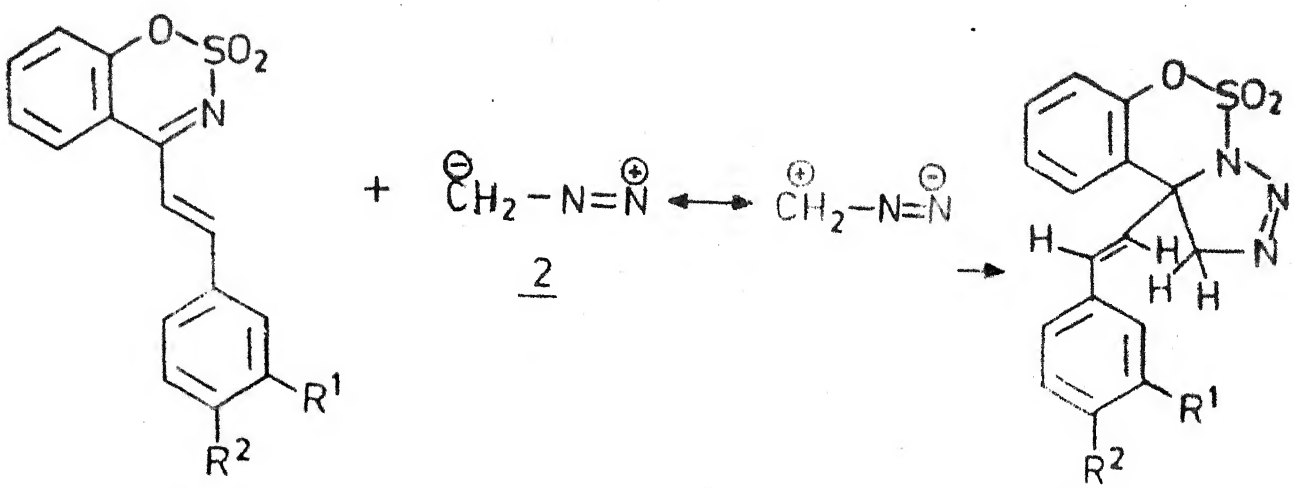
An addition of diazomethane across the C=C bond would give rise to two regio-isomers 5 and 6. In structure 5 the benzyl protons should come as a quartet around δ2.5. In structure 6 the benzyl protons should have appeared as a doublet around δ5 in the PMR spectrum. Thus structures 5 and 6 are also ruled out.


O
SO2
N
N
N
H
H
H
H
CH3
AROMATIC
+
OLEFINIC
METHYL
METHYLENE
TMS
7.5
6.5
2.4
1.4
PPM (δ)


O
SO2
N
N
N
CH2
CH3
1000
INTENSITY
0
%
3.0
0.0
117
132
160
183
196
224
50
100
150
200
M/E
277
(M+-SO2)
299
313 (M+-N2)
341 (M+)
250
300
350
400
450 M/E


100
80
60
40
20
0
TRANSMITTANCE (%)
3200
2800
1600
1400
1200
1000
800
WAVENUMBER (cm⁻¹)
1380 (SO2)
1165 (SO2)
O
SO2
N
N
N
H
H
H
H
CH3


-N2
-SO2
m/e 341(M+)
3 d
m/z 313
m/z 277
m/z 183
m/z 117
-CH2 N N
m/z 299
+
-SO2
m/z 224
-N2
m/z 160
m/z 196
-SO2
m/z 132

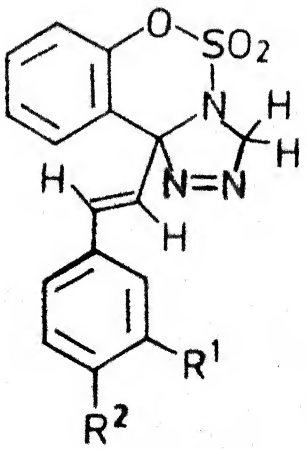


1 a-f

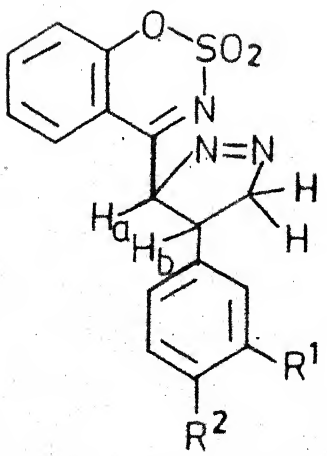
2

3 a-f

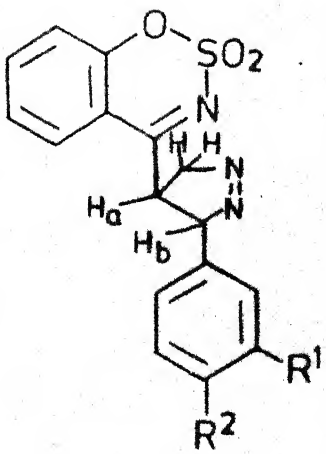
a : $R^1 = R^2 = H$
b : $R^1 = H$; $R^2 = Cl$
c : $R^1 = H$; $R^2 = Br$
d : $R^1 = H$; $R^2 = CH_3$
e : $R^1 = H$; $R^2 = OCH_3$
f : $R^1 = R^2 = OCH_3$



4 a-f



5 a-f



6 a-f

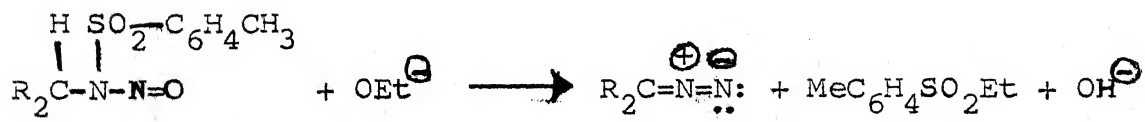
Thus reactions of various substituted 4-styryl-1,2,3-benzoxathiazene-2,2-dioxides (1a-f), with diazomethane gave the products (3a-f). The structures of (3a-f) were arrived at on the basis of IR, NMR and mass spectral data.

EXPERIMENTAL

The details of the equipments used for this investigation are same as described in the previous chapter.

STARTING MATERIALS

Various N-nitroso-N-alkyl compounds undergo elimination to give diazoalkanes. One of the most convenient methods is the *in situ* generation of diazomethane by the interaction of N-nitroso-N-methyl-p-toluene sulfonamide with a base. Thus:



where,

R = H

Preparation of 4-styryl-1,2,3-benzoxathiazine-2,2-dioxides

It was prepared by the method described in Part A of this chapter.

Reaction of 4-styryl-1,2,3-benzoxathiazine-2,2-dioxides with diazomethane

Excess of diazomethane was bubbled into a stirred solution of 1 (0.285g) (0.001 mol) in dichloromethane - ether mixture (1:1, 5 ml) at room temperature (~16°). The reaction mixture was allowed to stand for 30 minutes. The solvent was removed under reduced pressure. The silica gel chromatography of the residue, using benzene as an eluent, afforded the pure compound.

Yield	:	0.268g (82%), m.p. 150°.
Calcd for $C_{16}H_{13}N_3O_3S$	:	C: 58.71; H: 3.97; N: 12.84
Found	:	C: 58.78; H: 3.84; N: 12.93%
IR spectrum (KBr) ν_{max}	:	2980 (ν_{C-H}), 1380, 1150 (ν_{SO_2}) cm^{-1}.
PMR spectrum ($CDCl_3$), δ ppm	:	1.4 (q, 2H, $C\underline{H}_2$-N=N), 7.0-7.6 (m, 9H aromatic + 2H olefinic).
Mass spectrum	:	m/z: 327 (M^+).

Reaction of (1b) with diazomethane

The reaction of (1b) (0.319g, 0.001 mol) with diazomethane

was carried out, using the same procedure as described earlier, to give (3b). Yield, 0.285g (79%), m.p. 145°.

Calcd for $C_{16}H_{12}ClN_3O_3S$	:	C: 53.11; H: 3.31; N: 11.61
Found	:	C: 53.29; H: 3.42; N: 11.69%
IR spectrum (KBr) ν_{max}	:	2975 (ν_{C-H}), 1385, 1165 (ν_{SO_2}) cm^{-1}.
PMR spectrum ($CDCl_3$), δ ppm	:	1.6 (q, 2H, CH_2-N=N), 7.1-7.7 (m, 8H aromatic, 2H olefinic).
Mass spectrum	:	m/z: 361 (M^+).

Reaction of (1c) with diazomethane

The reaction of (1c) (0.364g, 0.001 mol) with diazomethane was performed in the usual manner to afford (3c). Yield, 0.345g (85%), m.p. 135°.

Calcd for $C_{16}H_{12}BrN_3O_3S$	:	C: 47.29; H: 2.95; N: 10.34
Found	:	C: 47.41; H: 2.83; N: 10.42%
IR spectrum (KBr), ν_{max}	:	2990 (ν_{C-H}), 1390, 1170 (ν_{SO_2}) cm^{-1}.
PMR spectrum ($CDCl_3$), δ ppm	:	1.5 (q, 2H, CH_2-N=N), 7.2-7.8 (m, 8H aromatic + 2H olefinic).
Mass spectrum	:	m/z: 406 (M^+).

Reaction (1d) with diazomethane

The reaction of (1d) (0.299g, 0.001 mol) with diazomethane

was carried out using the same procedure as mentioned before. It gave (3d). Yield, 0.259g (76%), m.p. 140°.

Calcd for $C_{17}H_{15}N_3O_3S$	:	C: 59.82; H: 4.39; N: 12.31
Found	:	C: 59.91; H: 4.50; N: 12.49%
IR spectrum (KBr) ν_{max}	:	2970 (ν_{C-H}), 1380, 1165 (ν_{SO_2}) cm^{-1}
PMR spectrum ($CDCl_3$, δ ppm	:	1.4 (q, 2H, $C\underline{H}_2$-N=N), 2.4 (s, 3H, $C\underline{H}_3$), 6.8-7.5 (m, 8H aromatic + 2H olefinic).
Mass spectrum	:	m/z: 341 (M^+).

Reaction of (1e) with diazomethane

The reaction of (1e) (0.315g, 0.001 mol) with diazomethane was carried out in manner described earlier. It furnished the product, (3e). Yield, 0.278g (78%), m.p. 150°.

Calcd for $C_{17}H_{15}N_3O_4S$	:	C: 57.14; H: 4.20; N: 11.76
Found	:	C: 57.29; H: 4.08; N: 11.81%
IR spectrum (KBr) ν_{max}	:	2980 (ν_{C-H}), 1380, 1170 (ν_{SO_2}) cm^{-1}.

PMR spectrum ($CDCl_3$), δ ppm : 1.5 (q, 2H, $C\underline{H}_2$-N=N), 3.7(s, 3H, $OC\underline{H}_3$), 6.8-7.4 (m, 8H aromatic + 2H olefinic).

Mass spectrum : m/z: 357 (M^+).

Reaction of (1f) with diazomethane

The product (3f) was obtained by the interaction of (1f) (0.345g, 0.001 mol) with diazomethane, according to the procedure described earlier. Yield, 0.305g, (79%), m.p.145°.

Calcd for $C_{18}H_{17}N_3O_5S$: C: 55.81; H: 4.39; N: 10.85

Found : C: 55.90; H: 4.23; N: 10.99%

IR spectrum (KBr) ν_{max} : 2985(ν_{C-H}), 1385, 1175 (ν_{SO_2}) cm^{-1}.

PMR spectrum ($CDCl_3$), δ ppm : 1.5 (q, 2H, $C\underline{H}_2$-N=N), 3.7 (s, 3H, $OC\underline{H}_3$), 3.8 (s, 3H, $OC\underline{H}_3$), 7.1-7.8 (m, 7H aromatic + 2H olefinic).

Mass spectrum : m/z: 387 (M^+).

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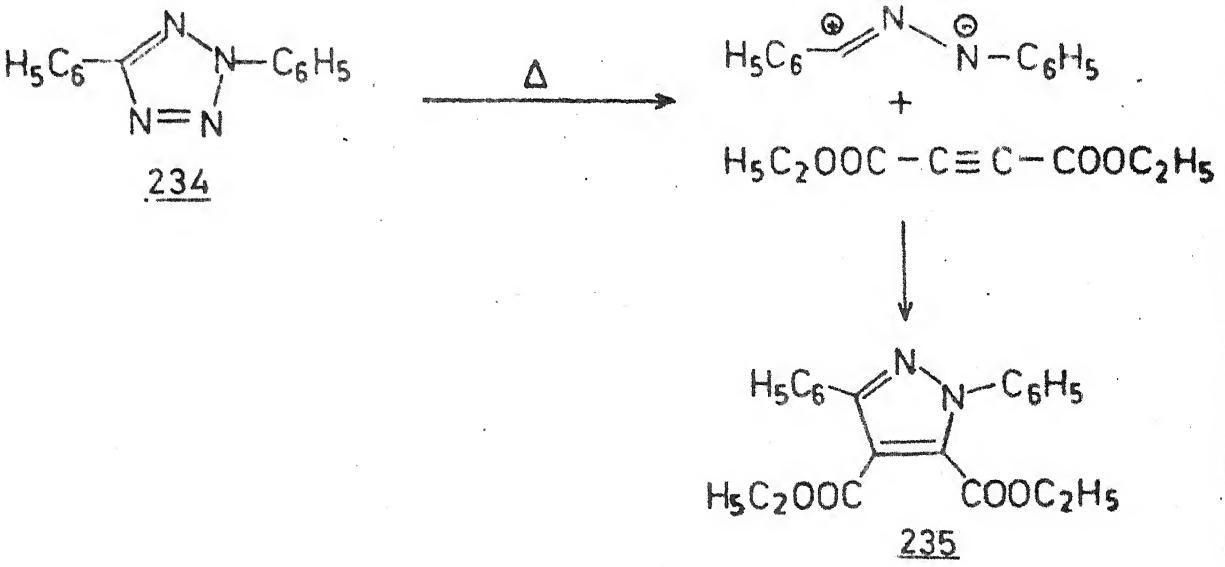
CHAPTER III

REACTIONS OF 1,2,3 BENZOXATHIAZINE-2,2-DIOXIDES WITH 1,3-DIPHENYLNITRILIMINE

Although the concept of 1,3-dipolar cycloaddition was postulated by Smith[1], the wide applicability of the reaction and its mechanism, have been the subject of brilliantly conceived and meticulously executed investigations of Huisgen and his coworkers.[2] The 1,3 dipolar addition offers a remarkably vast scope in the syntheses of 5 membered heterocycles. Second order kinetics, stereospecificity, regioselectivity and the conservation of orbital symmetry are some of the characteristics which these reactions exhibit, in accord with a one step four centre addition, in which the two bonds are formed simultaneously.[3] Since last few years, an increasing amount of work has been going on, which is apparent from the amount of literature available on this subject.[4-6] In 1,3 dipolar cycloaddition reactions, the 1,3 dipoles which are represented by resonance structures, combine with a dipolarophile to form a five membered heterocyclic system. 1,3 Diphenylnitrilimine forms a class of this type of reactive 1,3 dipole intermediates. Huisgen[7] et al. were the first to explore the reactivity of nitrilimines as a versatile 1,3 dipolar system in the syntheses of five membered heterocycles. An extensive study has been made by this group on the various aspects of this reactive intermediate, in a most systematic and elegant way.[1,2,7]

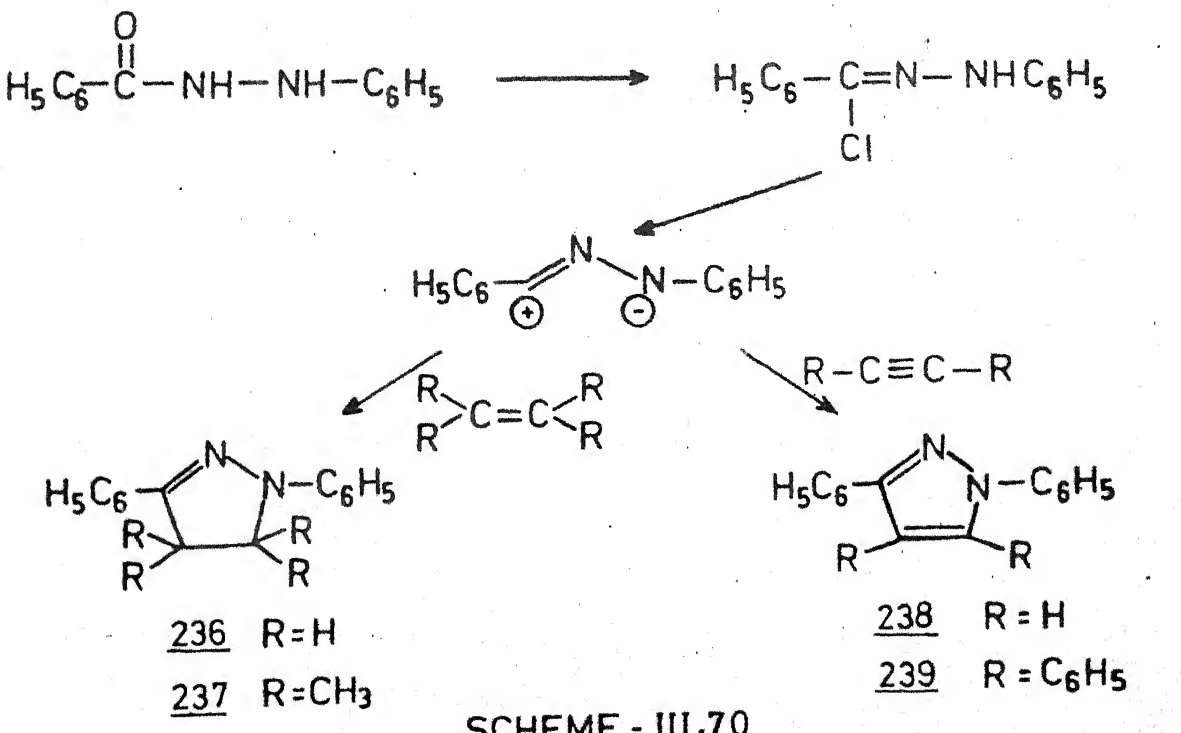
SCHEME - III.68



234

235

SCHEME - III.69



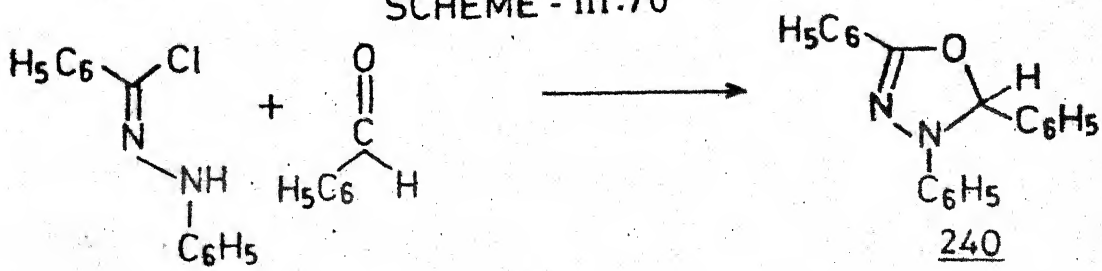
236 R=H

237 R=CH_3

238 R=H

239 R=C_6H_5

SCHEME - III.70



240

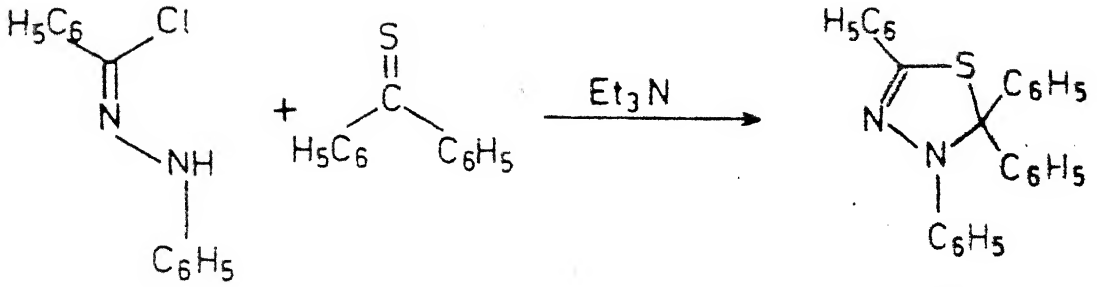
At first, 1,3 diphenylnitrilimines were prepared by Huisgen et al.[7] in situ by heating 2,5-diphenyl tetrazole(234) to 160°. The diphenylnitrilimine thus formed was made to react with various olefins to form 1,3-diphenylpyrazolines,[6,7] (235) (Scheme III.68).

In an attempt to discover an alternative method for the generation of 1,3 diphenylnitrilimine , the reaction of carboxylic acid hydrazide halides with triethylamine was found to be a better alternative over the other methods, since it allowed the generation of nitrilimine at ease, even at room temperature.[7,8]

N-Chlorobenzaldehyde phenyl hydrazone, the precursor of diphenylnitrilimine, is readily preparable by the reaction of PCl_5 on N-benzoyl-N'-phenyl hydrazine. Thus in situ generated diphenylnitrilimine , was made to react with various dipolarophiles viz., alkenes, alkynes to form the corresponding cyclo adducts (Scheme III.69).

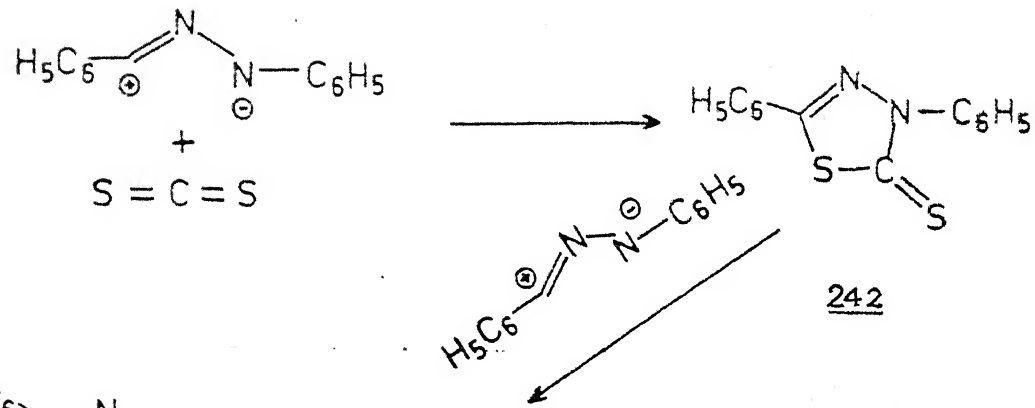
1,3-Diphenylnitrilimine is highly reactive and all attempts to isolate it proved unsuccessful. In the absence of a coreactant, it undergoes head to tail dimerisation to yield 1,4 dihydro-1,2,4,5-tetrazine. The cycloaddition reactions of nitrilimines can be classified on the basis of their ability to undergo intermolecular and intramolecular cycloaddition reactions. The cycloaddition, reactions of 1,3-diphenylnitrilimine (intermolecular type) are described in the following schemes.

SCHEME - III.71

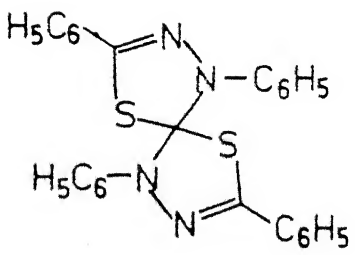


241

SCHEME - III.72



242



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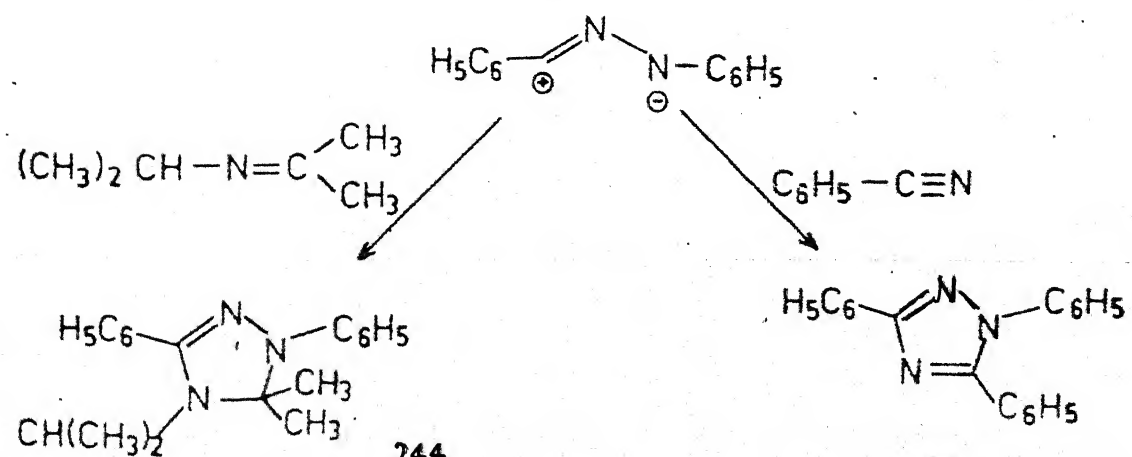
SCHEME - III.73



244

245

In a series of experiments Huisgen and his coworkers[1,2,8] found that 1,3-diphenylnitrilimines undergo stereospecific cis addition in their reactions with alkenes. It was concluded that conjugation increases the activity of the olefinic dipolarophile, though this is unexpected, since the alkene is deprived of its conjugation energy.

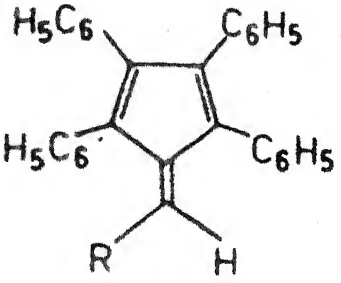
Apart from C-C multiple bonds, C=O bond also acted as a dipolarophile in many reactions. Thus benzaldehyde formed 2,4,5-triphenyl-1,3,4-oxadiazoline (240) with 1,3-diphenylnitrilimine (Scheme III.70). The reactivity of C=O[8] bond is less pronounced than that of C=C double bond in respect of cyclo-addition.

Thio compounds were found to be active dipolarophiles in their reactions with 1,3 dipoles. Thus, thio-benzophenone yielded thiadiazoline (241) with diphenylnitrilimine (Scheme III.71).

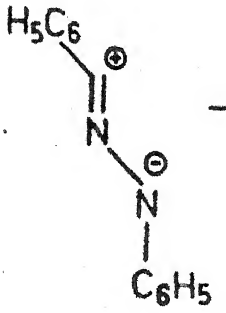
The reactivity of C=S bond was amply demonstrated by the facile reaction of CS_2 with 1,3 diphenylnitrilimine.[9] The primary adduct, cyclodithiourethane (242) afforded the 5,5-spiro bis-1,3,4-thiadiazoline on further reaction (Scheme III.72) with 1,3 diphenyl nitrilimine. The ease with which thio compounds add to diphenyl-nitrilimine may be result of high polarisibility of C=S bond.

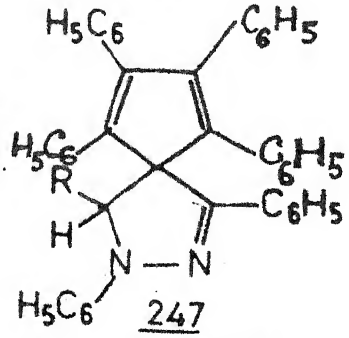
Aliphatic and aromatic azomethines add to diphenylnitrilimine to form 1,2,4-Δ^2-triazolines (244), while nitriles permit the synthesis of 1,2,4-triazoles (245). Thus the cyclo-addition reaction of

SCHEME - III.74



246



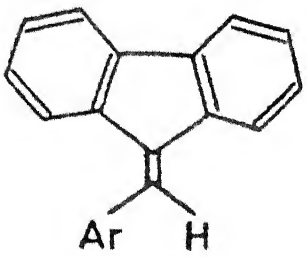


247

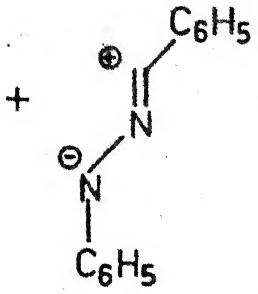
a R = H

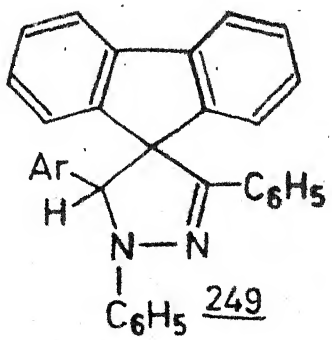
b R = CH_3

c R = C_6H_5



248



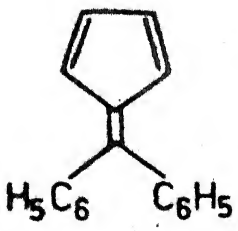


249

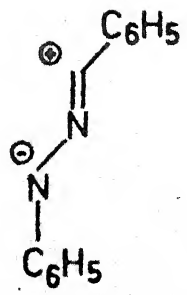
a Ar = C_6H_5

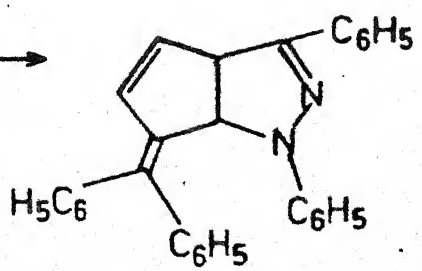
b Ar = p - ClC_6H_4

c Ar = p - MeC_6H_4



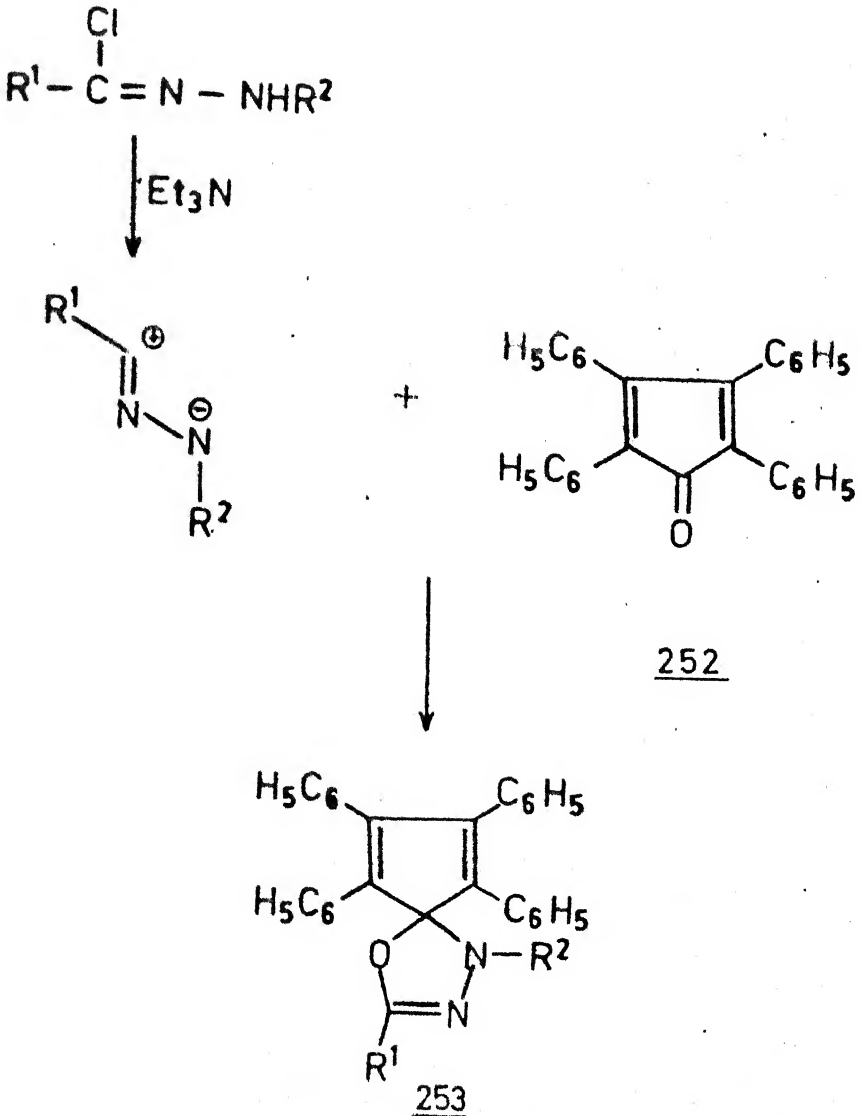
250





251

SCHEME - III.75



a $R^1 = R^2 = C_6H_5$

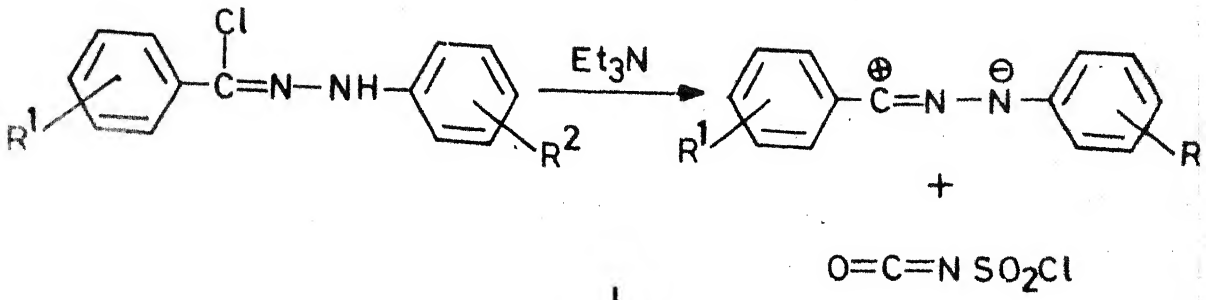
b $R^1 = \underline{p}\text{-}ClC_6H_4$, $R^2 = C_6H_5$

c $R^1 = \underline{p}\text{-}MeC_6H_4$, $R^2 = C_6H_5$

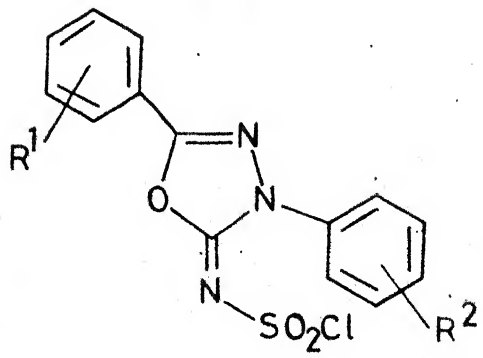
d $R^1 = \underline{p}\text{-}MeOC_6H_4$, $R^2 = C_6H_5$

e $R^2 = \underline{o}\text{-}ClC_6H_4$, $R^1 = C_6H_5$

Scheme III.76



254



255

a , $R^1 = R^2 = H$

b , R^1 = p-Cl ; $R^2 = H$

c , R^1 = p-Me ; $R^2 = H$

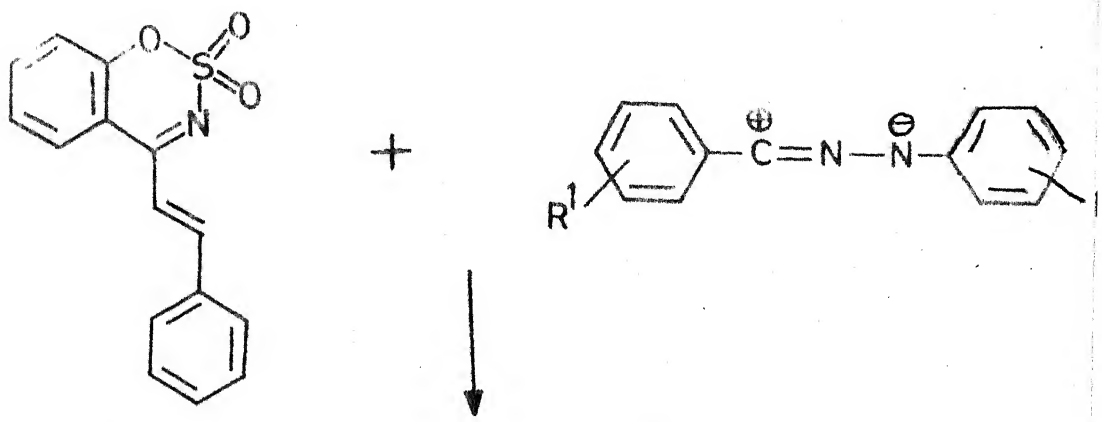
d , R^1 = p-OMe ; $R^2 = H$

e , $R^1 = H$; R^2 = O-Cl

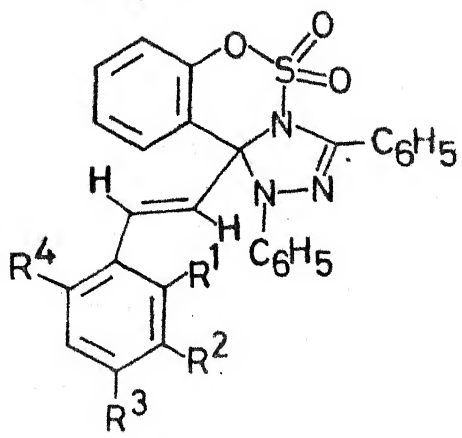
f , R^1 = m $-NO_2$; $R^2 = H$

g , R^1 = p $-NO_2$; $R^2 = H$

Scheme III.77



1a-e



256

a , $R^1 = R^2 = R^3 = R^4 = H$

b , $R^1 = R^2 = R^4 = H$; $R^3 = Cl$

c , $R^1 = R^4 = Cl$; $R^2 = R^3 = H$

d , $R^1 = R^2 = R^4 = H$; $R^3 = OMe$

e , $R^1 = R^4 = H$; $R^2 = R^3 = OMe$

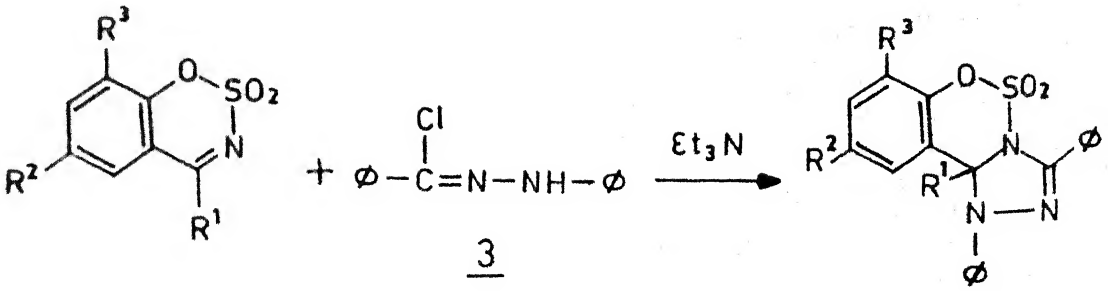
diphenylnitrilimines has enabled the synthesis of a wide range of heterocycles which are not easily accessible by other means. Thus it is interesting to observe the reactivity of this 1,3 dipole towards the polyolefins, for example, fulvenes. It has been shown that fulvenes[11] undergo addition across the exocyclic double bond with the exception of 6,6-diphenyl fulvene to yield the spiropyrazoline derivatives (247a-c). However, in the case of 6,6-diphenyl fulvene (250) a facile reaction takes place across the endocyclic C=C double bond to yield another pyrazoline derivative (251) (Scheme III.74).

1,3-Diarylnitrilimines[11] undergo addition across the C=O bond of tetracyclone (Scheme III.75).

1,3-Diarylnitrilimines have been reported[12] to react with chlorosulfonyl isocyanate to yield the oxadiazoline derivatives (255a-g) (Scheme III.76).

Reactions of benz-N-phenylhydrazidoyl chloride with (1a-e) in benzene at 50-60° in presence of triethylamine resulted in the formation of hitherto unreported heterocyclic system (256a-c) (Scheme III.77). In these reactions, diphenylnitrilimine add to the C=N moiety of the 4 styryl-1,2,3-benzoxathiazine-2,2-dioxides.

Thus the cyclo-addition reactions of diphenylnitrilimines have enabled the synthesis of a wide range of heterocycles, which are not easily accessible by other means. 1,2,3-Benzoxathiazine-2,2-dioxide forms an interesting class of substrates because



2 a-g

4 a-g

a : $R^1 = R^2 = R^3 = H$

b : $R^1 = R^3 = H$; R^2,= Br

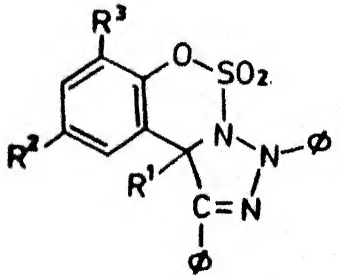
c : $R^1 = H$; $R^2 = R^3 = Br$

d : $R^1 = R^3 = H$, $R^2 = Cl$

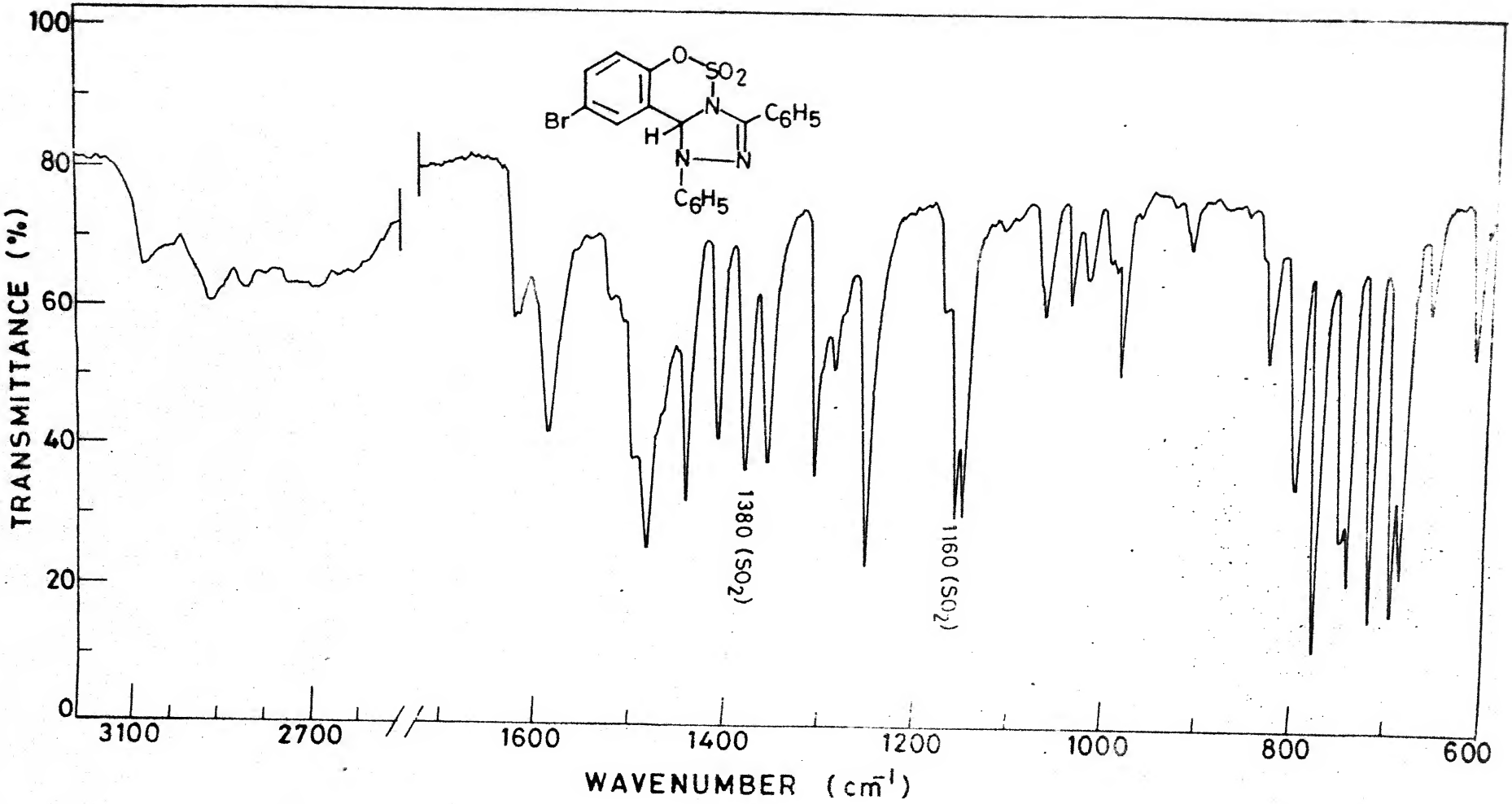
e : $R^1 = H$; $R^2 = R^3 = I$

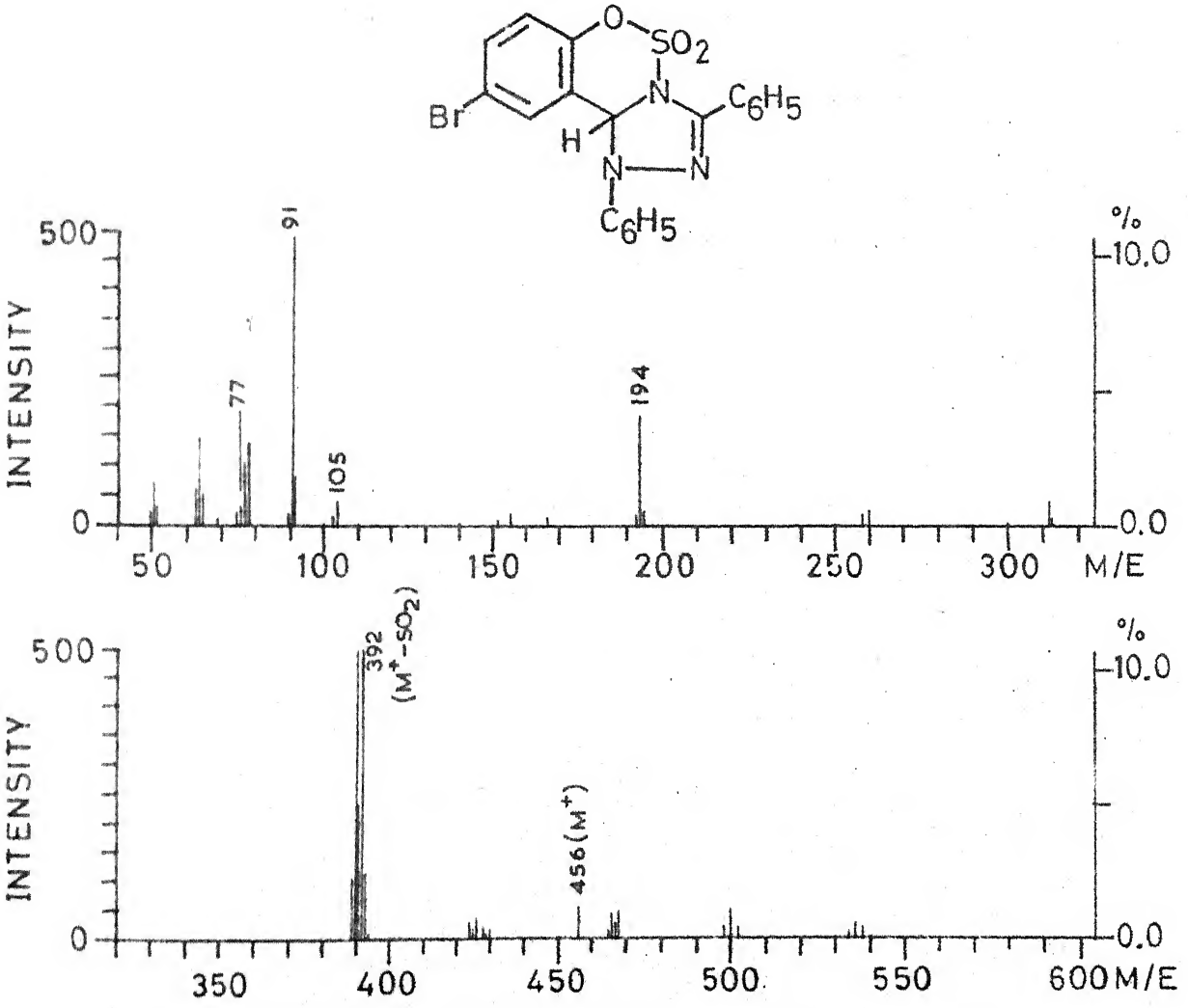
f : $R^1 = CH_3$; $R^2 = R^3 = H$

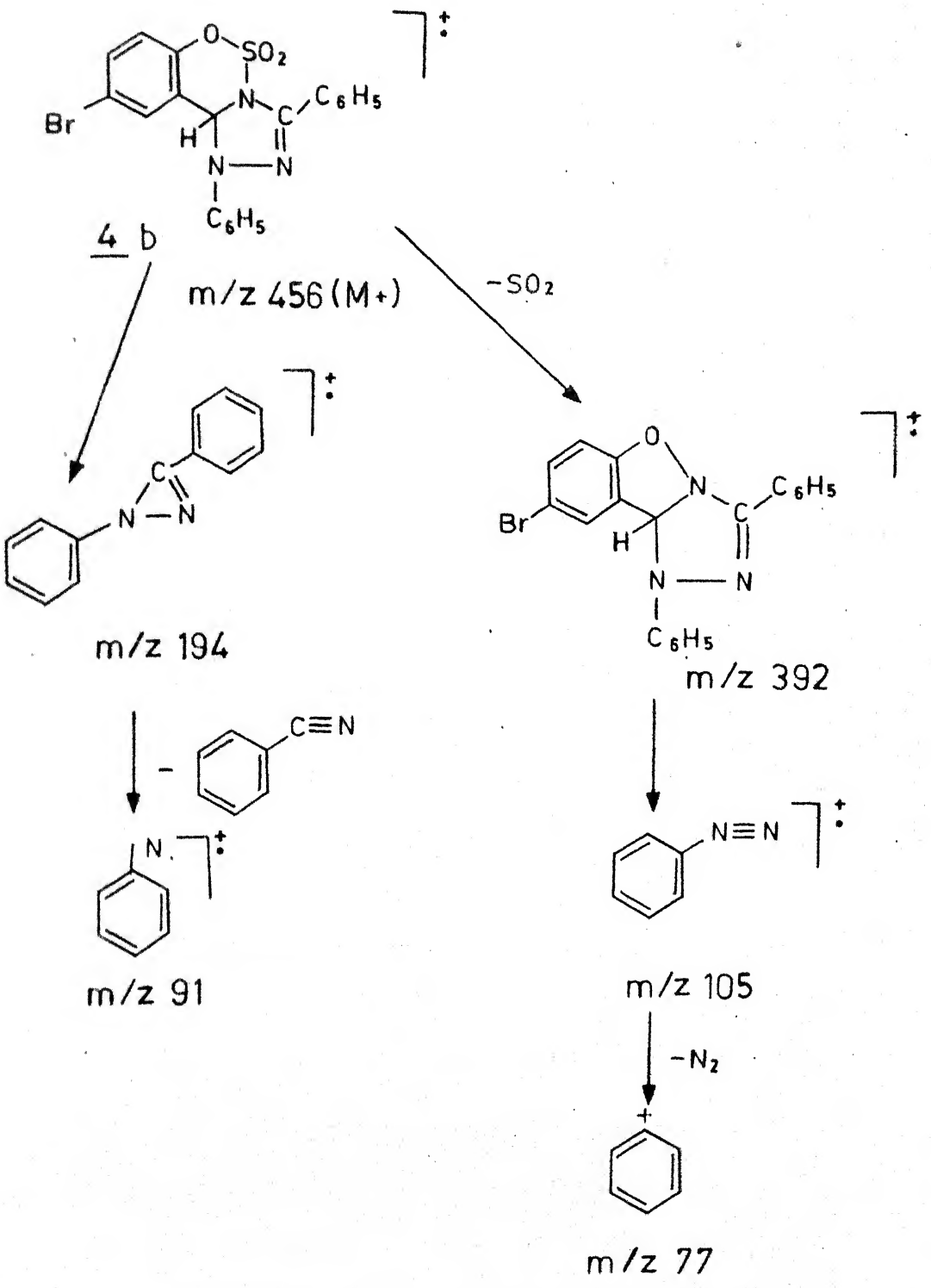
g : $R^1 = \emptyset$, $R^2 = R^3 = H$



5 a-g


100
80
60
40
20
0
TRANSMITTANCE (%)
3100
2700
1600
1400
1200
1000
800
600
WAVENUMBER (cm⁻¹)
1380 (SO2)
1160 (SO2)
Br
O
SO2
N
C6H5
H
N
N
C6H5


O
SO2
Br
N
C6H5
H
N
N
C6H5
500
INTENSITY
0
91
77
105
194
%
10.0
0.0
50
100
150
200
250
300
M/E
500
INTENSITY
0
392
(M+-SO2)
456(M+)
%
10.0
0.0
350
400
450
500
550
600
M/E


4 b
m/z 456 (M+)
-SO2
m/z 194
m/z 392
m/z 91
m/z 105
-N2
m/z 77

of their susceptibility to chemical attack at C=N position. 1,2,3-benzoxathiazine-2,2-dioxides (2a-g) are synthesized readily from their parent substituted salicylaldehydes and o-hydroxyacetophenones. An equimolar (1:1) quantity of salicylaldehyde or o-hydroxy acetophenone and chlorosulfonyl isocyanate is added in refluxing toluene. The reaction mixture is allowed to continue refluxing at the same temperature. The work-up of the reaction mixture affords 1,2,3-benzoxathiazine-2,2-dioxides.

RESULTS AND DISCUSSION

In an attempt to widen the scope of 1,3 dipolar cycloaddition in the syntheses of novel heterocyclic systems, a systematic study of the reactions of 1,3-diphenylnitrilimine with various substituted 1,2,3-benzoxathiazine-2,2-dioxides was undertaken. Reactions of Benz-N-phenyl-hydrazidoyl chloride with (2a-g) (in benzene in the presence of triethylamine at 50-60°) resulted in the formation of hitherto unreported heterocyclic system (4a-g). 1,3-Diphenylnitrilimine (generated *in situ*) adds to the >C=N- group of these compounds, to furnish the tricyclic system (4a-g).

The IR spectrum exhibits bands at ν1380 and ν1150 cm^{-1} due to the presence of SO_2 group. In the PMR spectrum all the protons show up as a complex multiplet in the aromatic region δ 6.4-8.2. The formation of the regio-isomer (5) in the above reaction has been ruled out on the basis of PMR data. The benzylic proton in (5)

should have appeared as a singlet around δ 5.5-6.0. The mass-fragmentation pattern is also in agreement with the proposed structure.

EXPERIMENTAL

All the melting points are uncorrected and were taken on Fischer-Johns melting point apparatus. Infra red spectra were recorded in Perkin Elmer-580 spectrophotometer. PMR spectra were taken in Jeol JMS-300D spectrometer. Elemental analyses were carried out on Coleman carbon, hydrogen and nitrogen automatic analysers.

STARTING MATERIALS

Preparation of Benz-N-phenylhydrazidoyl chloride

The titled compound was prepared in accordance with the procedure described in the literature.[7] To a suspension of 1-N-benzoyl-2-N-phenylhydrazine (8g) in dry ether (30 ml) was added phosphorus pentachloride (10g) and the mixture was refluxed for 10 h. To the clear solution obtained, phenol (16g) was added slowly followed by methanol (20 ml). The main part of the ether

was evaporated by raising the temperature ($\sim 40^{\circ}$) and the solution on cooling gave a yellow solid. This was filtered and recrystallised from methanol to give colorless crystals (5g), m.p., 128° (lit.[7] m.p. 129°).

5-Bromosalicylaldehyde

Salicylaldehyde (40g) was dissolved in acetic acid (130 ml). The reaction mixture was treated with hydrobromic acid (85 ml) at 35°. Sodium chlorate (11.2g) in 25 ml of water was added to this mixture during 90 minutes (40°). It was recrystallized from ethanol m.p., 106° (lit.[13] m.p. 104.5°).

3,5-Dibromosalicylaldehyde

Salicylaldehyde (15g) was treated with acetic acid (75 ml). To this solution hydrobromic acid (65 ml) was added. This whole reaction mixture was treated with sodium chlorate (8.4g) in 15 ml of water between 30-40°. This afforded 3,5-dibromosalicylaldehyde, which was recrystallized with ethanol. m.p. 85° (lit.[13] mp. 84.6°).

5-Chlorosalicylaldehyde

Glycerol (150g) and boric acid (35g) were heated for 30 minutes at 170° (to expel all water) then, at 170°, hexamethylene tetraamine (25g) was added. The mixture was stirred and brought

to 160°, the phenol (25g) added without delay and the temperature maintained at 150-155° for 15 minutes (with stirring). The thick brown liquid was left to cool to 110°, a solution of conc. sulfuric acid (30 ml), in water (100 ml) was added. This whole mixture was boiled in a current of steam. The solid p-chlorosalicylaldehyde was practically pure when collected. m.p. 98° (lit.[14], m.p. 99°).

3,5-Diiodosalicylaldehyde

Salicylaldehyde (30g) was mixed with a solution of 1N-NaOH (250 ml) containing some Na_2CO_3 (225 ml, 30%), followed by the addition of iodine, (130g) in KI solution (prepared by dissolving 200g KI, in 100 ml water). After standing for 24 h. the product (as sodium salt) was filtered, washed and crystallized from hot water. The free aldehyde was regenerated by acidification (HCl) of the product. It was recrystallized from 60% ethanol. m.p. 108°.

Synthesis of 1,2,3-Benzoxathiazine-2,2-dioxides[15] (General method): (o-Hydroxy acetophenone, Salicylaldehyde)

To a stirred solution of the 2-hydroxy compounds (0.046 mol) in toluene (40 ml) at 100-105° was added chlorosulfonyl isocyanate (4 ml, 0.046 mol) in toluene (5 ml) over a period of 20 minutes. Stirring was continued for 3 h at the same temperature. Solvent was distilled off under diminished pressure

and the residue obtained was diluted with ice-cold water (50 ml). The desired product was filtered, washed with water, and recrystallized from ethanol.

Reactions of 1,2,3-Benzoxathiazine-2,2-dioxides (108a-g) with Benz-N-phenylhydrazidoyl chloride (General Method)

Dry triethylamine (0.3 ml) was added to a stirred solution of (2a-g) (0.001 mol) and benz-N-phenylhydrazidoyl chloride[9] (0.203g, 0.001 mol) in dry benzene (10 ml). The solution was stirred for 36 h at 50-60°, filtered to remove triethylamine hydrochloride. The filtrate was evaporated to yield a crude solid. It was purified by passing its benzene solution through a silica gel column.

Synthesis of (4a) : Yield: 0.358g (95%), m.p. 155°.

Calcd for $C_{20}H_{15}N_3O_3S$: C: 63.66; H: 3.97; N: 11.14

Found : C: 63.51; H: 3.88; N: 11.20%

IR spectrum (KBr) ν_{max} : 1620 (C=N), 1385, 1165(ν_{SO_2}) cm^{-1}.

PMR spectrum ($CDCl_3$), δ ppm : 6.4-8.2 (m, 15H).

Mass spectrum : m/z: 377 (M^+), 313 (M^+-SO_2).

Synthesis of (4b) : Yield: 0.373g (82%), m.p. 200°.

Calcd for $C_{20}H_{14}BrN_3O_3S$: C: 52.63; H: 3.07; N: 9.21

Found : C: 52.67; H: 3.12; N: 9.13%

IR spectrum (KBr) ν_{max} : 1620(C=N), 1380,1160(ν_{SO_2}) cm^{-1}.

PMR spectrum ($CDCl_3$), δ ppm : 7.0-8.0 (m, 14H).

Mass spectrum : m/z: 456 (M^+), 392 (M^+-SO_2).

Synthesis of (4c) : Yield: 0.454g (85%), m.p. 210°.

Calcd for $C_{20}H_{13}Br_2N_3O_3S$: C: 44.85; H: 2.42; N: 7.85

Found : C: 44.79; H: 2.50; N: 7.71%

IR spectrum (KBr) ν_{max} : 1615(C=N), 1380,1160(ν_{SO_2}) cm^{-1}.

PMR spectrum ($CDCl_3$), δ ppm : 7.1-8.0 (m, 13H).

Mass spectrum : m/z: 535 (M^+), 491 (M^+-SO_2).

Synthesis of (4d) : Yield: 0.337g (82%), m.p. 202°.

Calcd for $C_{20}H_{14}ClN_3O_3S$: C: 58.32; H: 3.40; N: 10.20

Found : C: 58.27; H: 3.52; N: 10.28%

IR spectrum (KBr) ν_{max} : 1615 (C=N), 1385, 1165(ν_{SO_2}) cm^{-1}.

PMR spectrum ($CDCl_3$), δ ppm : 7.0-8.0 (m, 14H).

Mass spectrum : m/z: 411(M^+), 337 (M^+-SO_2).

Synthesis of (4e) : Yield: 0.60g (85%), m.p. 240°.

Calcd for $C_{20}H_{13}I_2N_3O_3S$: C: 33.85; H: 1.83; N: 5.92

Found : C: 33.78; H: 1.91; N: 5.83%

IR spectrum (KBr) ν_{max} : 1610(C=N), 1380, 1160(ν_{SO_2}) cm^{-1}.

PMR spectrum ($CDCl_3$), δ ppm : 7.1-8.2 (m, 13H).

Mass spectrum : m/z: 709 (M^+), 645 (M^+-SO_2).

Synthesis of (4f) : Yield: 0.336g (86%), m.p. 180°.

Calcd for $C_{21}H_{17}N_3O_3S$: C: 64.45; H: 4.34; N: 10.74

Found : C: 64.36; H: 4.41; N: 10.77%

IR spectrum (KBr) ν_{max} : 1615(C=N), 1380, 1150 (ν_{SO_2}) cm^{-1}.

PMR spectrum ($CDCl_3$), δ ppm : 2.0 (s, 3H, CH_3), 7.0-8.0 (m, 14H, aromatic).

Mass spectrum : m/z: 391 (M^+), 317 (M^+-SO_2).

Synthesis of (4g)	:	Yield: 0.394g (87%), m.p. 190°.
Calcd for $C_{26}H_{19}N_3O_3S$	:	C: 68.87; H: 4.19; N: 9.27
Found	:	C: 68.69; H: 4.01; N: 9.41%
IR spectrum (KBr) ν_{max}	:	1615(C=N), 1385, 1155(ν_{SO_2}) cm^{-1}.
PMR spectrum ($CDCl_3$), δ ppm	:	7.1-8.2 (m, 19H).
Mass spectrum	:	m/z: 453 (M^+), 389 (M^+-SO_2).

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CHAPTER IV

CERIC AMMONIUM NITRATE OXIDATION OF 4-PHENYL-Δ'-[1,2,4]-TRIAZOLINE-5-THIONES, 3H-1,2-BENZODITHIOLE-3-THIONES AND FLAVANONES

Ceric ammonium nitrate oxidation of various substituted 4-phenyl-Δ'-[1,2,4]triazoline-5-thiones, 3H-1,2-benzodithiole-3-thiones and flavanones were investigated. The 5-thiones taken up for the present study include, 3,3-dimethyl-4-phenyl-Δ'-[1,2,4]-triazoline-5-thione (5a), 3-ethyl, 3-methyl-4'-phenyl-Δ'-[1,2,4]-triazoline-5-thione (5b), cyclohexanespiro-3'-(4'-phenyl-Δ'-[1',2',4']triazoline-5'-thione)(5c), cyclopentane spiro -3'-(4'-phenyl-Δ'-[1',2',3']triazoline-5'-thione) (5d), 3,3-diethyl-4-phenyl-Δ'-[1,2,4]-triazoline-5-thione (5e). The other thiones investigated are the various p-chlorophenyl substituted triazoline-5-thiones (5f-j). CAN converts these thiones into their corresponding triazoline-5-ones (332a-j) in excellent yields. In addition, the reaction of CAN with 3H-1,2-benzodithiole-3-thiones furnish their corresponding benzodithiole-3-ones in very good yields. The substrates taken for the present investigation include 3H-1,2-benzodithiole-3-thione (327a). 5-methyl,3H-1,2-benzodithiole (327b), 7-methyl, 3H-1,2-benzodithiole (327c), 5,7-dichloro (327d), 5-chloro, 3H-1,2-benzodithiole (327e), 3-thiones. Flavanones are cleaved by CAN to give a new class of heterocyclic compounds. The compounds used for this study include flavanone, 4-methyl-flavanone, 4'-methoxy flavanone and 3',4'-dimethoxy flavanone. In all these cases compounds (333a-d) were obtained.

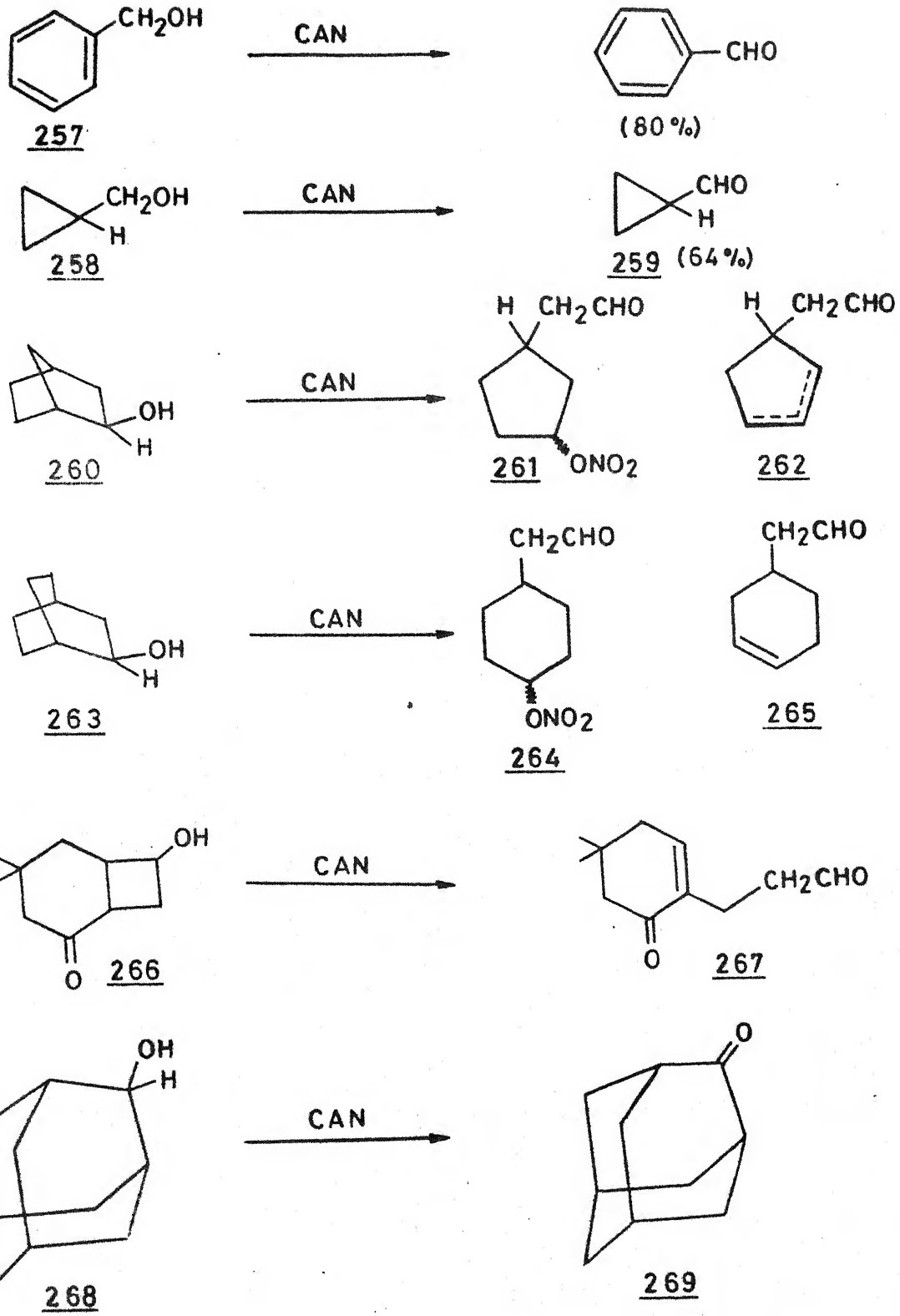
Another oxidant, pyridine chlorochromate, is found to react with various 4-phenyl-Δ^1-[1,2,4]triazoline-5-thiones. Their corresponding triazoline-5-ones are obtained in very good yields.

Ceric ion in its various coordination states has been known as a strong oxidising agent for many decades.[1] However, early use of ceric ion in organic chemistry was primarily restricted to colorimetric and quantitative estimation of alcohols.[2] Later studies[1] revealed the ability of ceric ion to oxidise a variety of organic functional groups but these efforts were mostly devoted to the studies of reaction kinetics and little effort was expended to the preparative aspects of these reactions. Investigations during the last decade by Trahanovsky[3] and others[4] on ceric ammonium nitrate (CAN) and ceric ammonium sulfate (CAS) oxidation of a number of organic compounds have drawn attention to the synthetic versatility of ceric ion in preparative organic chemistry.[4] Consequently, a great deal of promising synthetic methodology has been revealed[4] by employing ceric ions. In the following text the oxidation of common organic functional groups with ceric reagents is discussed.

ALCOHOLS

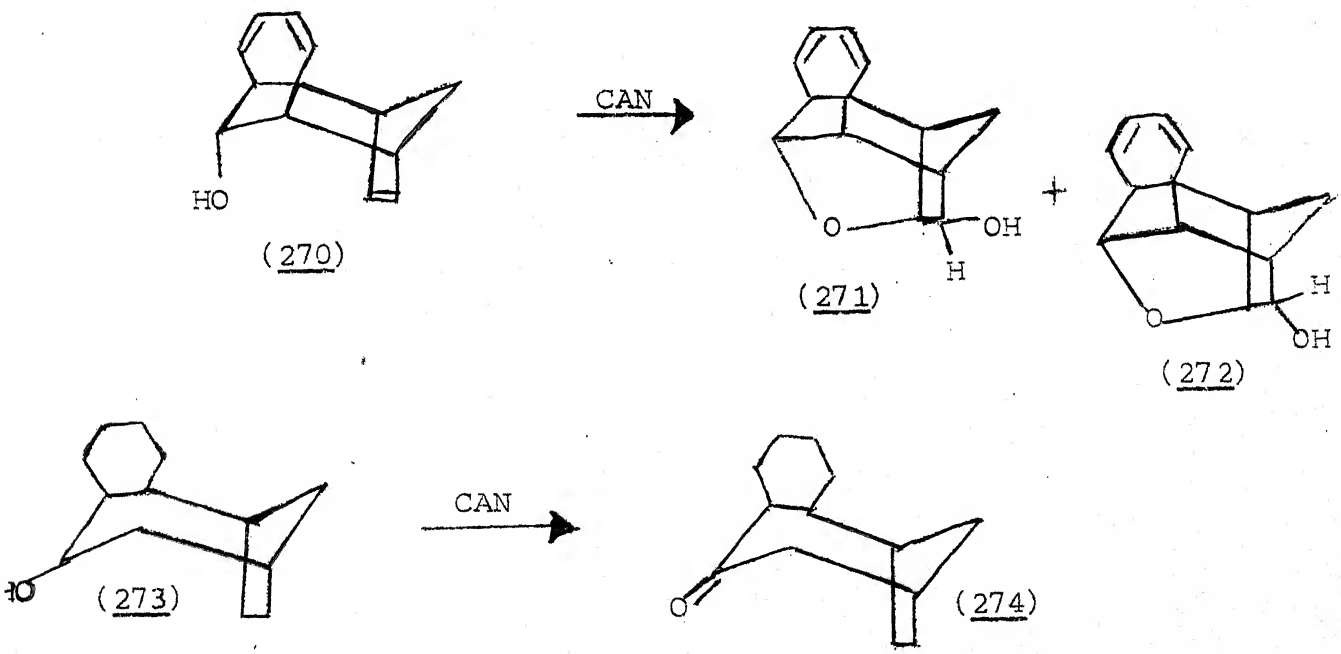
Among the various functional groups, alcohols are most readily oxidised by ceric ion and their reactions have been extensively studied. Thus benzylic[5] and cyclopropyl carbinyl[6]

Scheme IV.78


CH2OH
CAN
CHO
257
(80 %)
CH2OH
H
CAN
CHO
H
258
259 (64 %)
OH
H
CAN
H CH2CHO
ONO2
H CH2CHO
260
261
262
OH
H
CAN
CH2CHO
ONO2
CH2CHO
263
264
265
OH
CAN
CH2CHO
O
266
267
OH
H
CAN
O
268
269

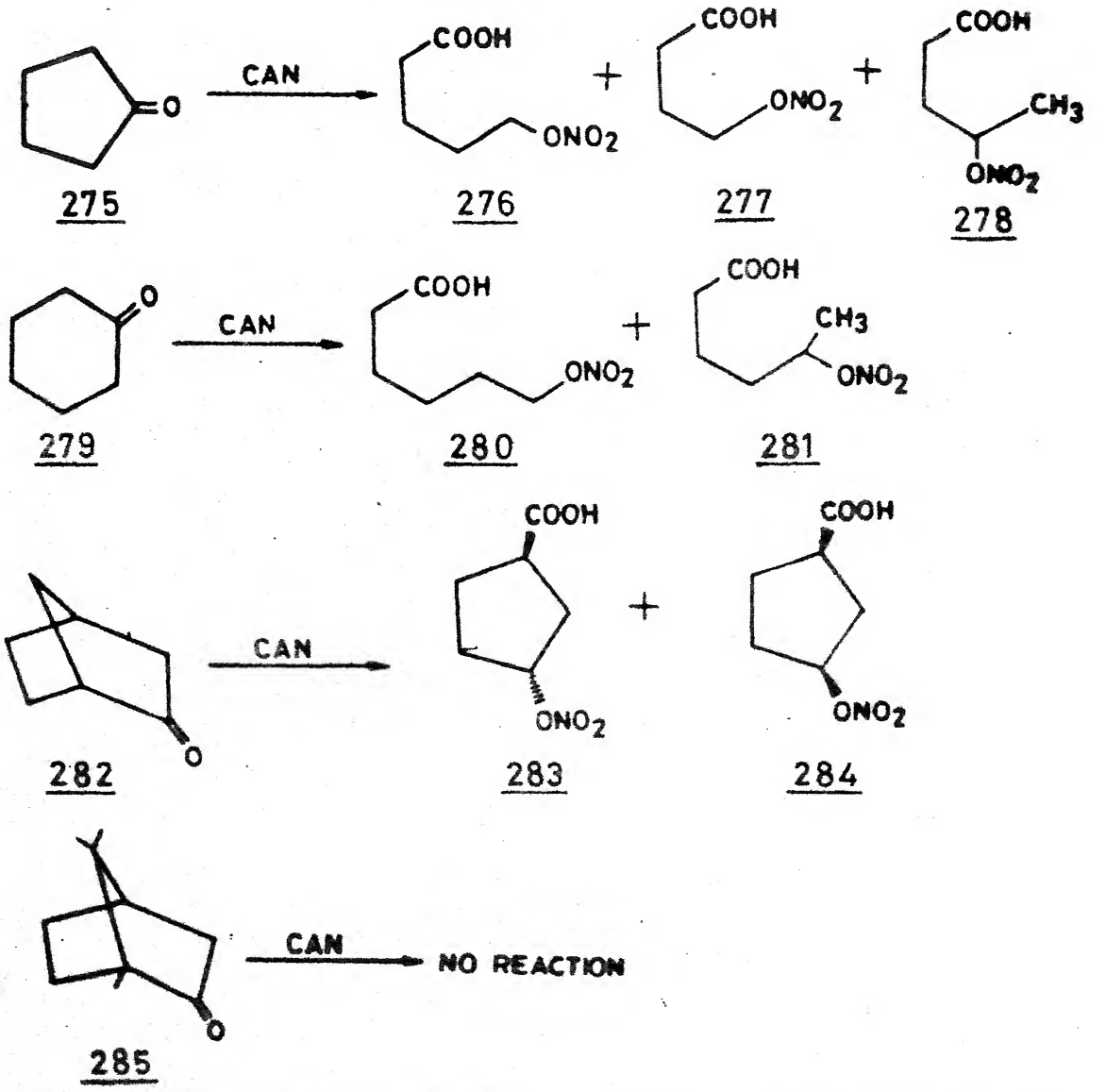
alcohols are oxidised to the corresponding aldehydes. Bridged alcohols and cyclobutanols[8] are oxidised with adjacent C-C bond fission. α-glycols are cleaved[9] by ceric ion and alkanols possessing a δ-hydrogen atom such as n-pentanol[10], produce tetrahydrofuran derivatives in analogy with lead tetraacetate oxidations. Simple cyclic alcohols like cyclopentanol and cyclohexanol as well as adamantanol are dehydrogenated[11] to the corresponding ketones in the presence of ceric ion. These reactions with typical illustrations are depicted in Scheme IV.78. Mechanistic studies,[8,12] have suggested that ceric ion induced alcohol cleavage is one electron process, whereas for ketone formation a two electron oxidation is operative. The cyclization of bridged secondary alcohols[17] with ceric ammonium nitrate is shown in Scheme IV.79 Aryl methanols on treatment with sodium bromate and catalytic amount of ceric ammonium nitrate[14] give the corresponding carbonyl compounds.

Scheme IV.79

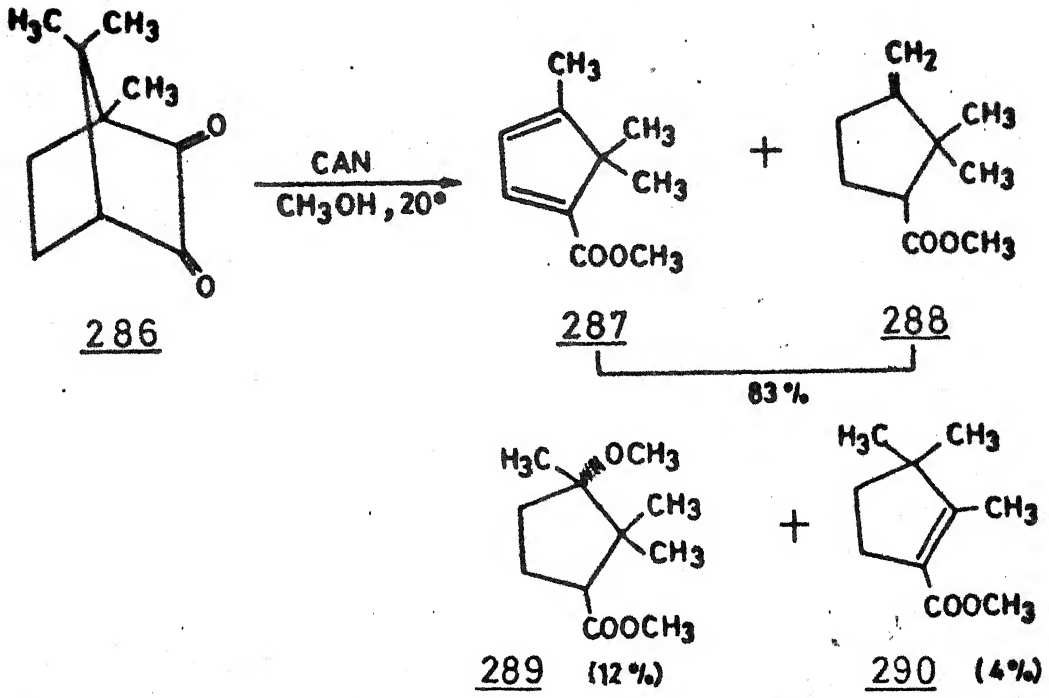


(270) (271) (272) (273) (274)

Scheme IV.80


CAN
COOH
ONO2
CH3
275
276
277
278
279
280
281
282
283
284
285
NO REACTION

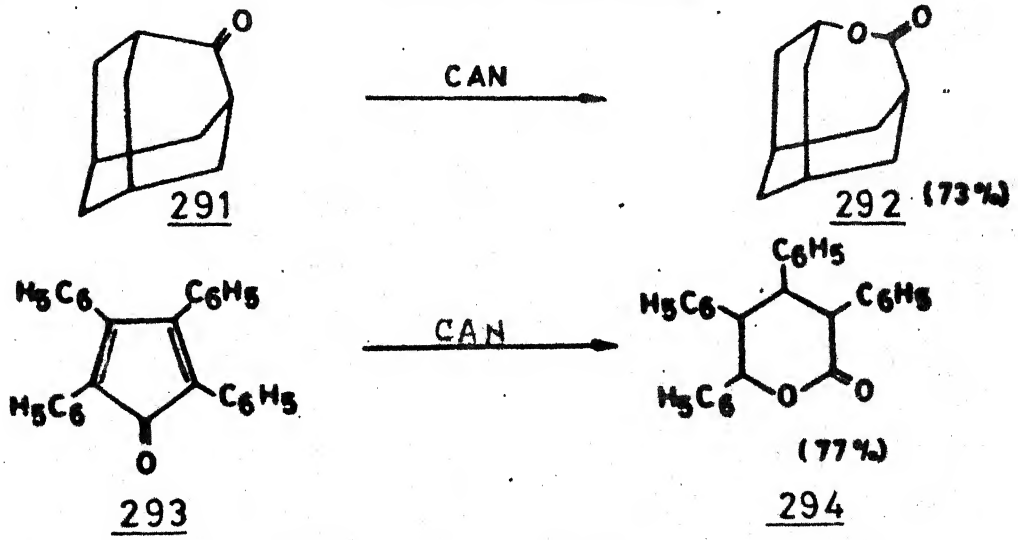
SCHEME IV.81



286 → 287 + 288

289 (12%) + 290 (4%)

SCHEME IV.82



291 → 292 (73%)

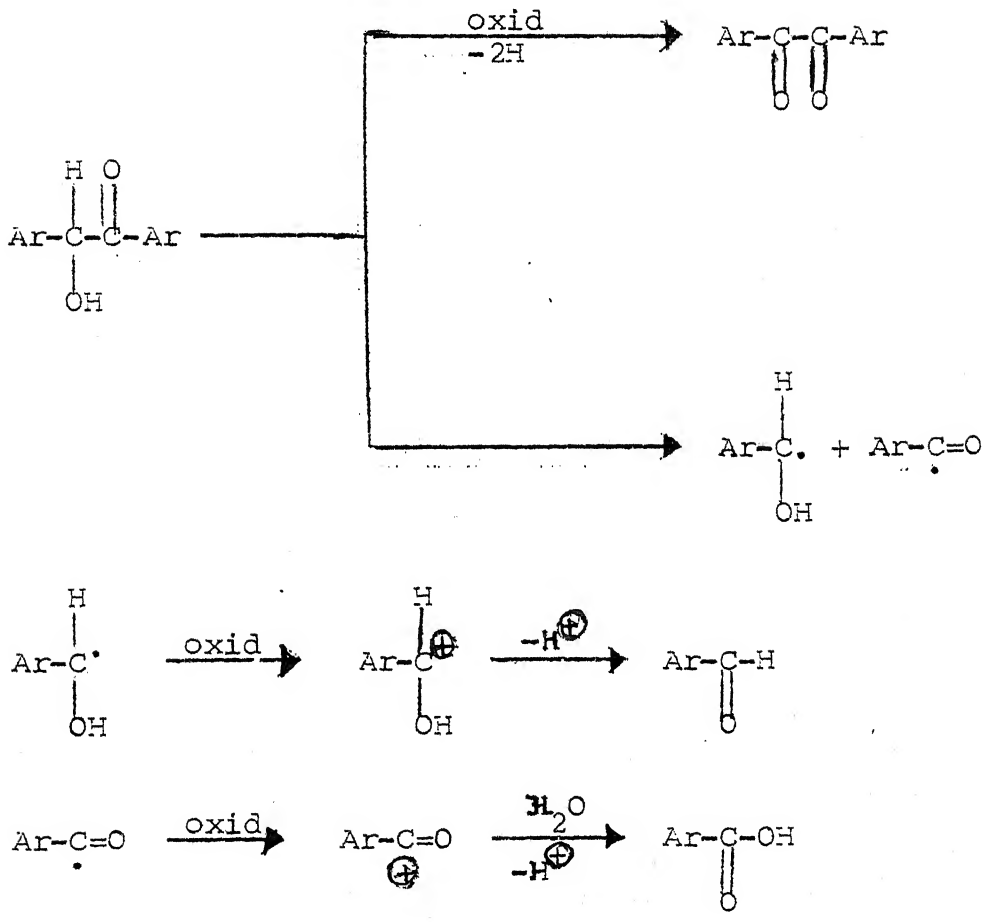
293 → 294 (77%)

Ceric ammonium nitrate absorbed on activated charcoal[15] has been found to be an efficient catalyst for the air oxidation of benzyl alcohols and acyloins to the corresponding carbonyl compounds.

CARBONYL COMPOUNDS

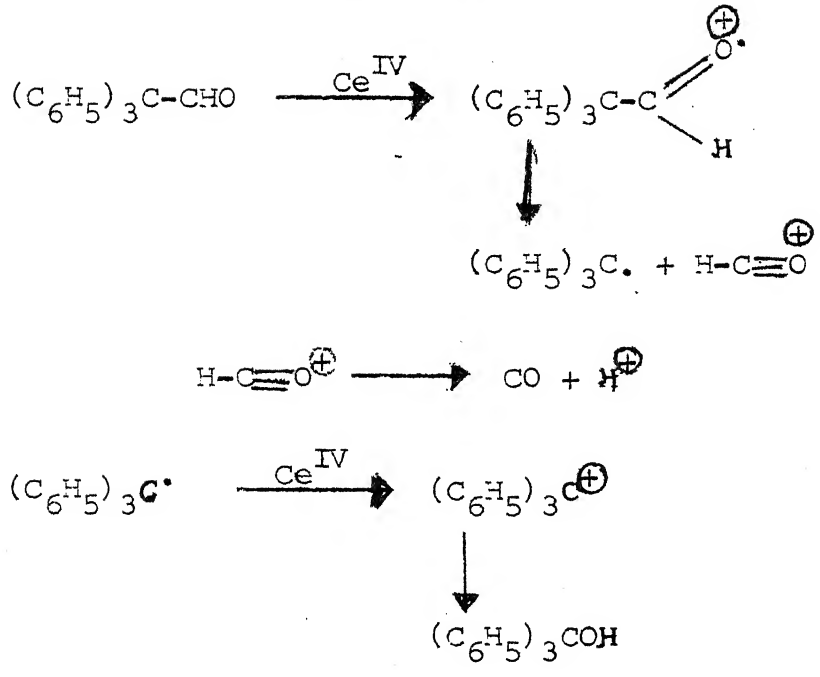
Alicyclic ketones are rapidly consumed by CAN or ceric ammonium sulfate to furnish the corresponding nitratocarboxylic acid *via* a pathway involving α-cleavage.[16] Cyclopentanone, cyclohexanone and norbornanone belong to this category and furnish mixtures of ring opened carboxylic acids (Scheme IV.80). Camphor itself is not effected by treatment with CAN in methanol at 20°, but the nonenolizable camphorquinone (286) is oxidised easily, mainly to an inseparable mixture of (287) and (288)[17] (Scheme IV.81). Adamantanone (291) and tetracyclone (293) exhibit unexpected behaviour towards CAN and undergo efficient Baeyer Villiger oxidation[16,4], to the lactone (292) and tetraphenyl α-pyrone (294) (Scheme IV.82). Benzoin[17] splits into benzaldehyde and benzoic acid (yield: 86%) when treated with CAN in aqueous acetonitrile (*vide* Scheme IV.83).

Scheme IV.83



Aldehydes and ketones[17] are susceptible to ceric ion oxidation. Formaldehyde, for example, is oxidized to formic acid (in acid media). It was reported that the reaction with triphenyl acetaldehyde gave triphenyl carbinol together with some unreacted aldehyde, and the reaction was interpreted as proceeding via hydrogen abstraction .

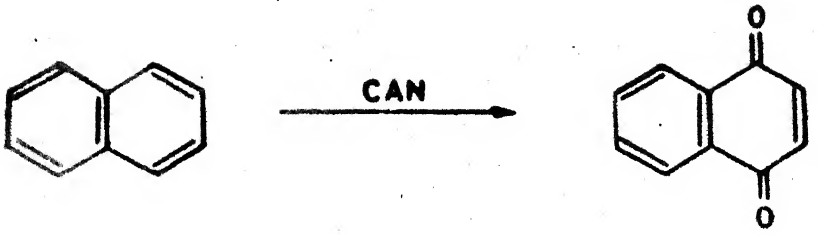
Scheme IV.86



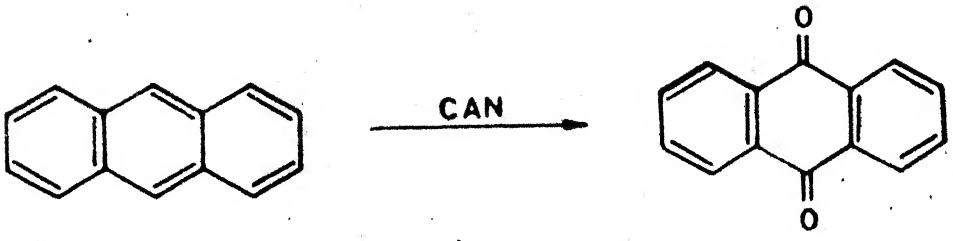
Carboxylic acids

Simple aliphatic and aromatic carboxylic acids are usually stable towards ceric ion. However, oxalic acid[18] and malonic acid[19] are readily oxidized by ceric ion to carbon dioxide and water. The higher homologues of these dicarboxylic acids do not react with ceric ion. Cycloheptatriene carboxylic acid (295) is readily decarboxylated to tropylium salt (296) with CAN in 30% yield.[20]

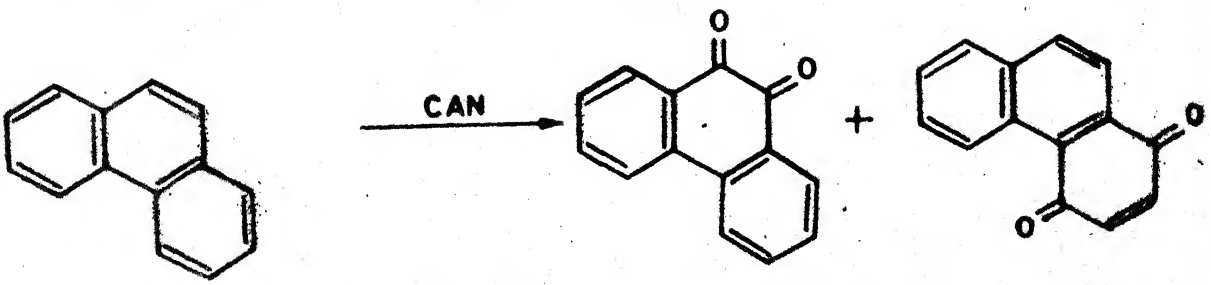
Scheme IV.89



298 299

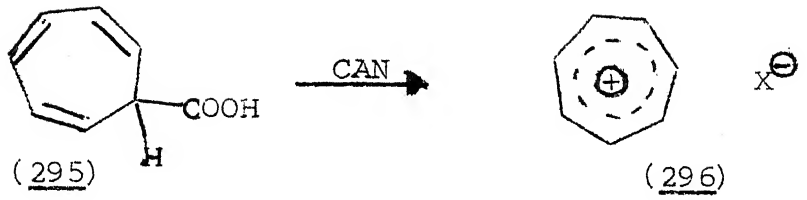


300 301



302 303 304

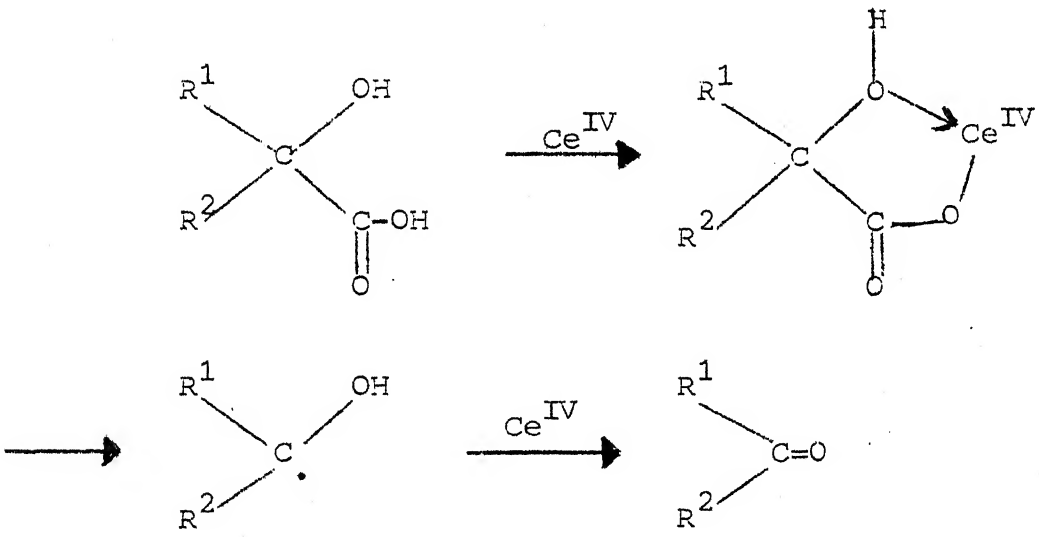
Scheme IV.87



(295) (296)

α-hydroxy carboxylic acids are degraded[21] to carbonyl compounds with loss of a carbon atom by ceric ion and this contributes a useful degradative method.

Scheme IV.88

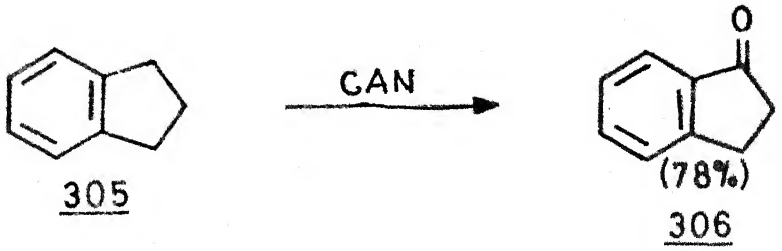


(297) (100%)

HYDROCARBONS

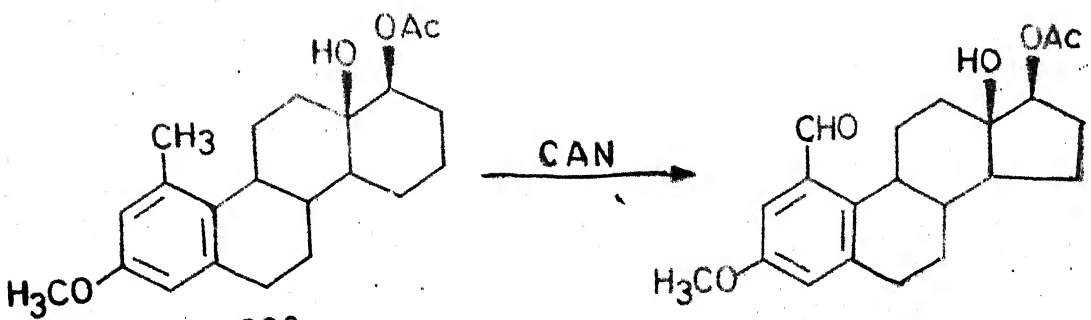
Aromatic hydrocarbons, possessing benzylic methyl and methylene groups, are readily oxidized to corresponding carbonyl functions by CAN in acidic medium.[22] Thus o- and p- xylenes are

Scheme IV.90

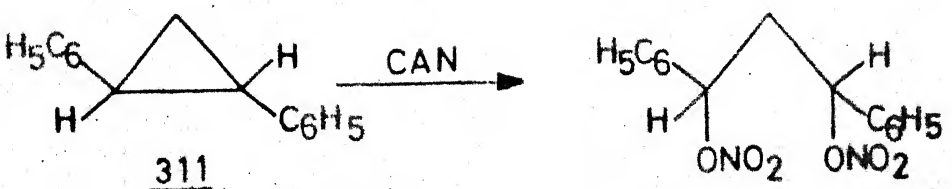


305 306

307 308

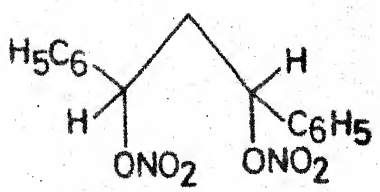


309 310



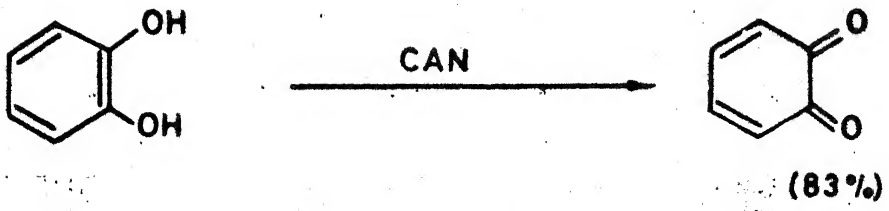
311 312

+



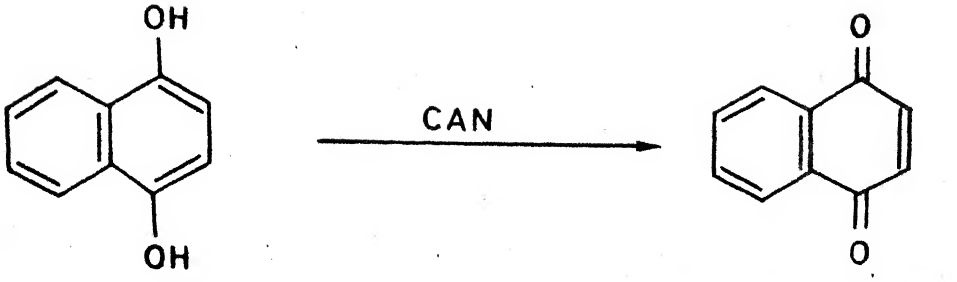
313

Scheme IV.91



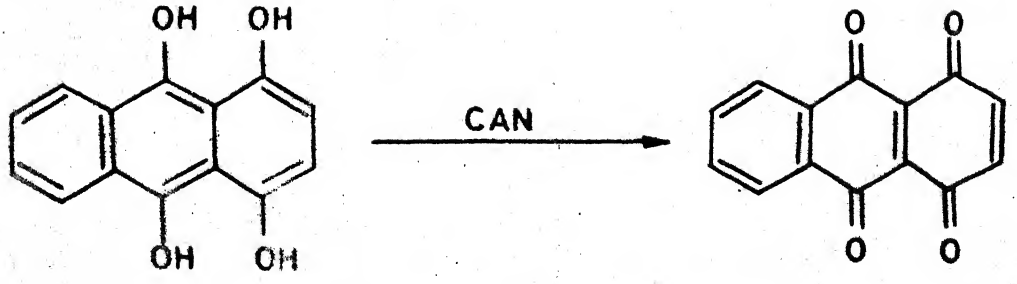
(83%)

314 315



(88%)

316 317



318 319 (89%)

oxidized to 2- and 4-methyl-benzaldehydes respectively in 100% yield.[18] Polynuclear hydrocarbons are readily oxidized[23] to quinones by CAN under mild conditions and in good yields (Scheme IV.89).

Efficient conversion of indane(305) to 1-indanone (306), tetralin (307) to 1-tetralone (308) and steroidal[24] substrate (309) to (310) are useful examples of hydrocarbon oxidation (Scheme IV.90)

Aryl cyclopropanes like (311) are cleaved[25] by CAN in acetic acid to ring open products (312) and (313). Oxidation of 1,2-diaryl ethanes[26] with CAN produce only cleavage product: benzaldehyde, benzyl alcohol and benzyl nitrate (vide infra).

$$ArCH_2CH_2Ar \xrightarrow{CAN} \underset{60\%}{ArCHO} + \underset{30\%}{ArCH_2OH} + \underset{10\%}{ArCH_2ONO_2}$$

HYDROQUINONES

Hydroquinones can be rapidly and efficiently oxidized[27] to the corresponding quinones by CAN. The oxidation procedure is applicable for the generation of ortho-, para- and diquinones (Scheme IV.91).

Oximes and semicarbazones

In many synthetic operations, it is expedient to either protect on purify carbonyl compounds via their oxime and

semicarbazone derivatives. CAN regenerates[28] the parent ketones or aldehydes from oximes and semicarbazones, at low temperature ar in excellent yields and thus it provides a superior and mild alter native to the conventionally used regeneration procedures.

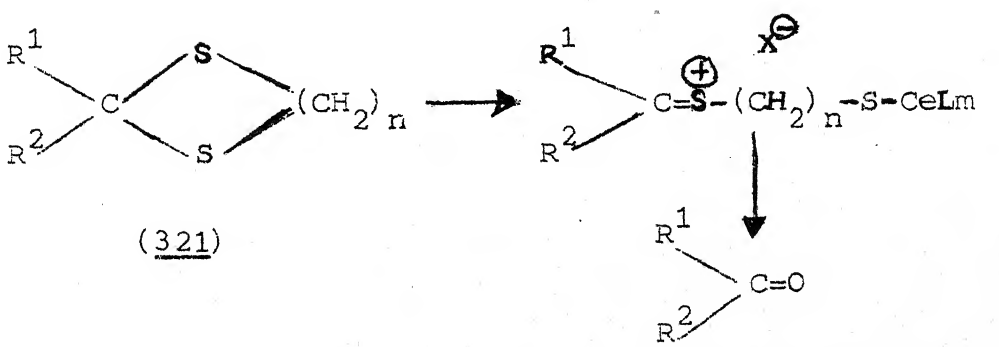
ORGANO-SULFUR COMPOUND

Diaryl sulfides are readily oxidized to the corresponding sulfoxides[25] in high yields without any contamination with the corresponding sulfones (vide infra).

(320)

The oxidation of sulfides to sulfoxides[29] can be carried out with catalytic amount of CAN and sodium bromate in aceto-nitrile.[30] 1,3-Dithiolanes and dithianes are readily degraded to their parent carbonyl compounds[31] on treatment with CAN. The reaction may be visualized to take place as shown:

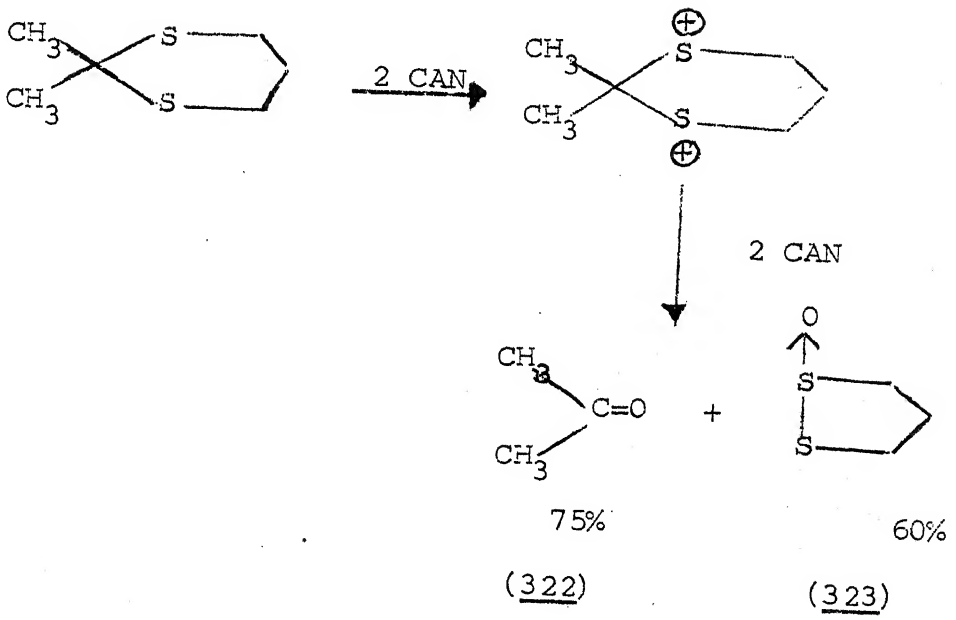
Scheme IV.92



(321)

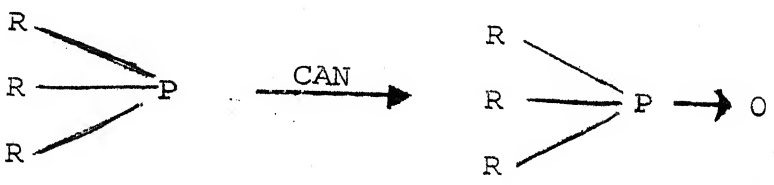
The cleavage of 1,3-dithianes by CAN[32] requires four equivalents of the oxidant for obtaining high yield of the products (vide Scheme IV.93).

Scheme IV.93

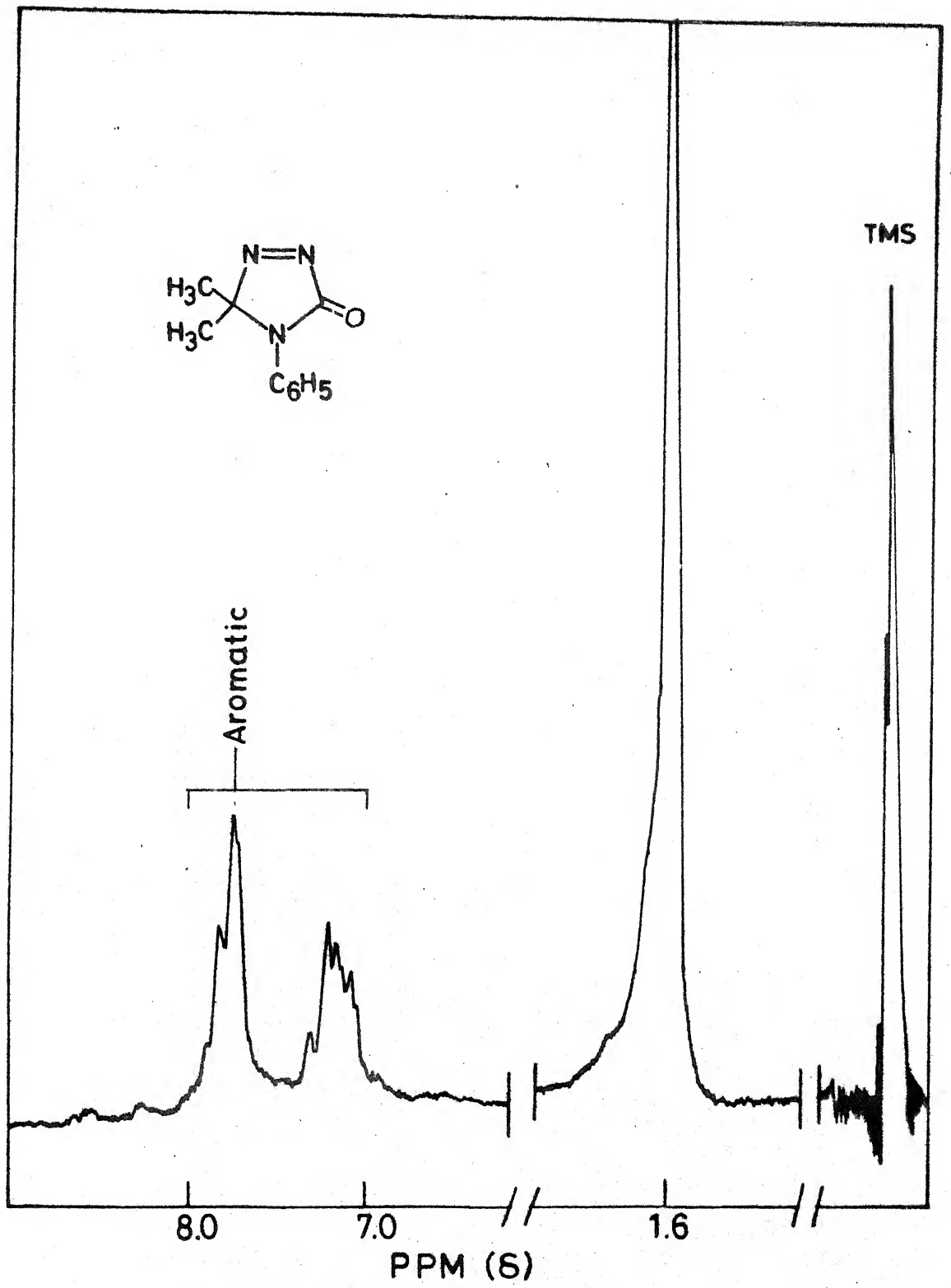


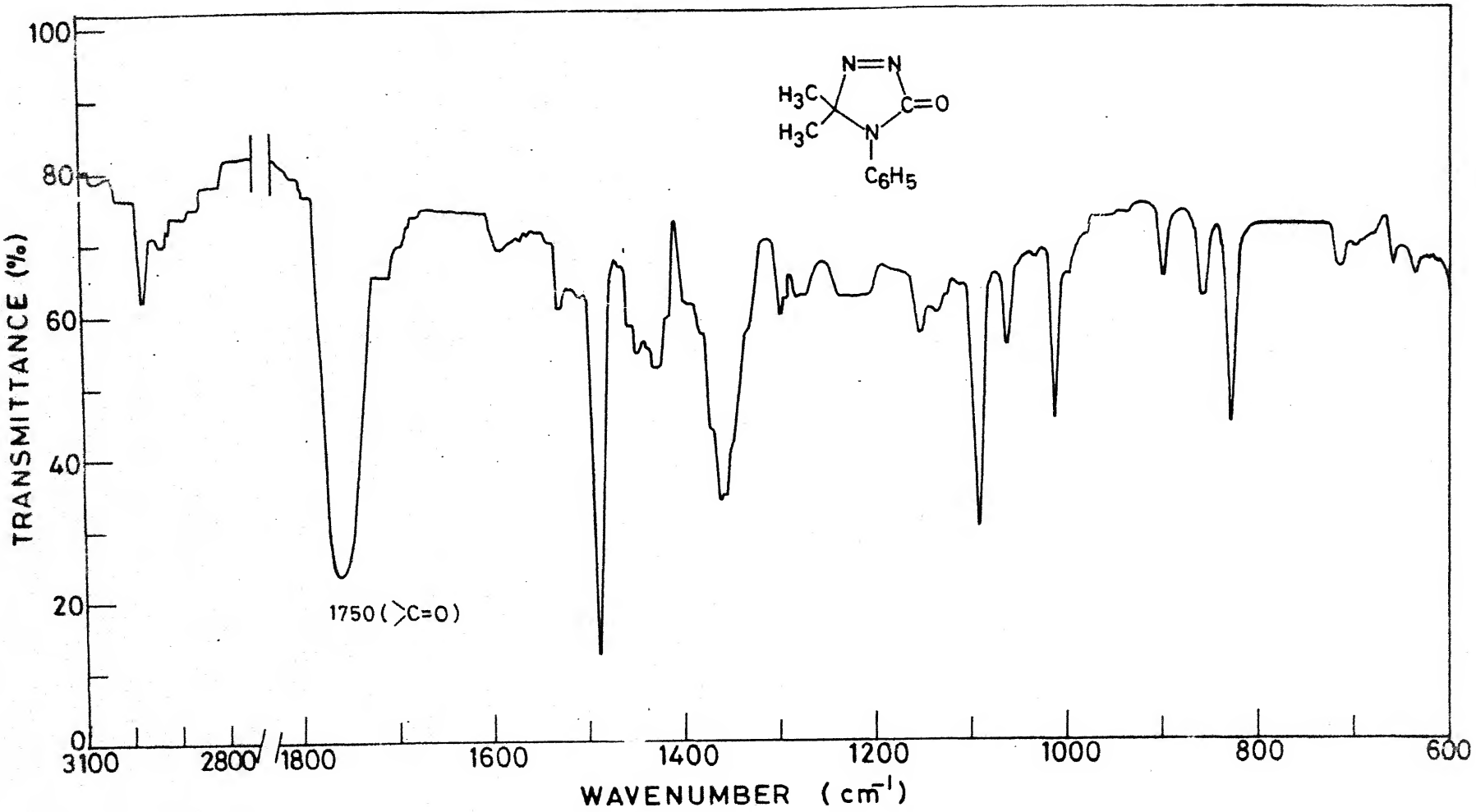
(322) (323)

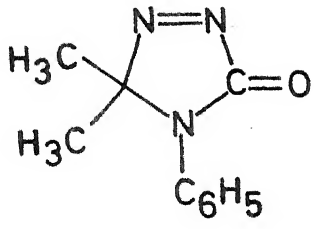
Phosphines are quantitatively transformed to the corresponding phosphine oxides by ceric ion.[4] (vide infra).

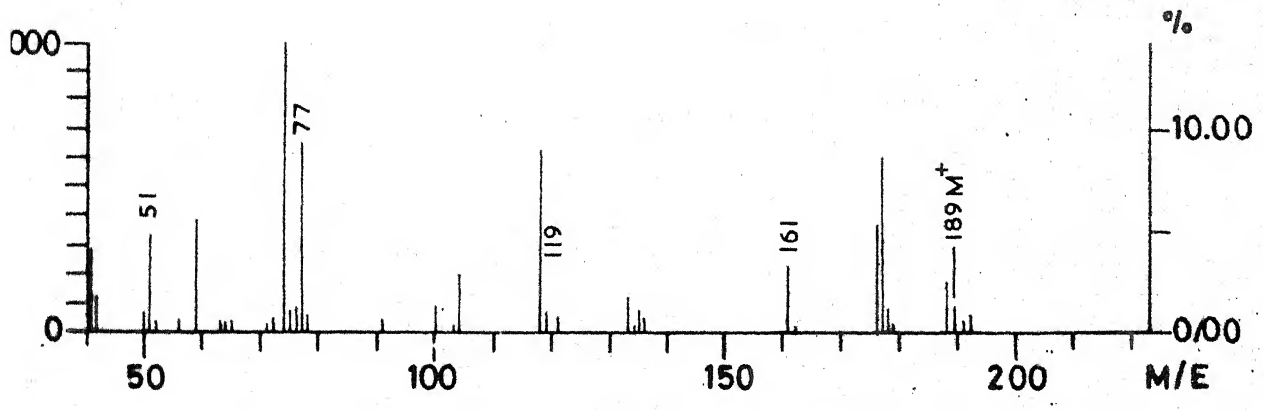


(324) (325)


N=N
H3C
H3C
O
N
C6H5
TMS
Aromatic
8.0
7.0
1.6
PPM (δ)


100
80
60
40
20
0
TRANSMITTANCE (%)
3100
2800
1800
1600
1400
1200
1000
800
600
WAVENUMBER (cm⁻¹)
1750 (>C=O)
N=N
H3C
H3C
C=O
N
C6H5


N=N
H3C
C=O
N
H3C
C6H5


000
0
%
10.00
0.00
51
77
119
161
189 M+
50
100
150
200
M/E

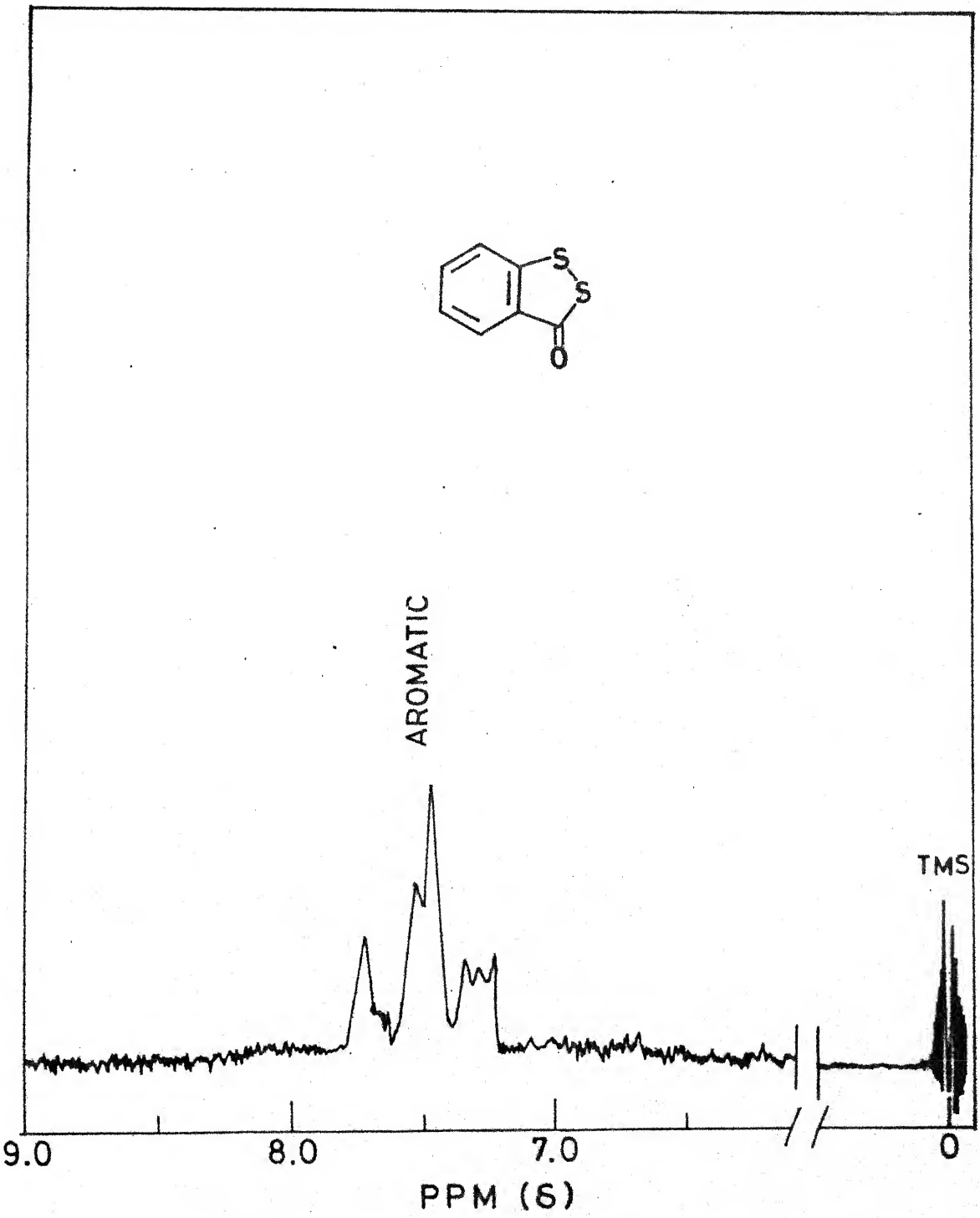
RESULTS AND DISCUSSION

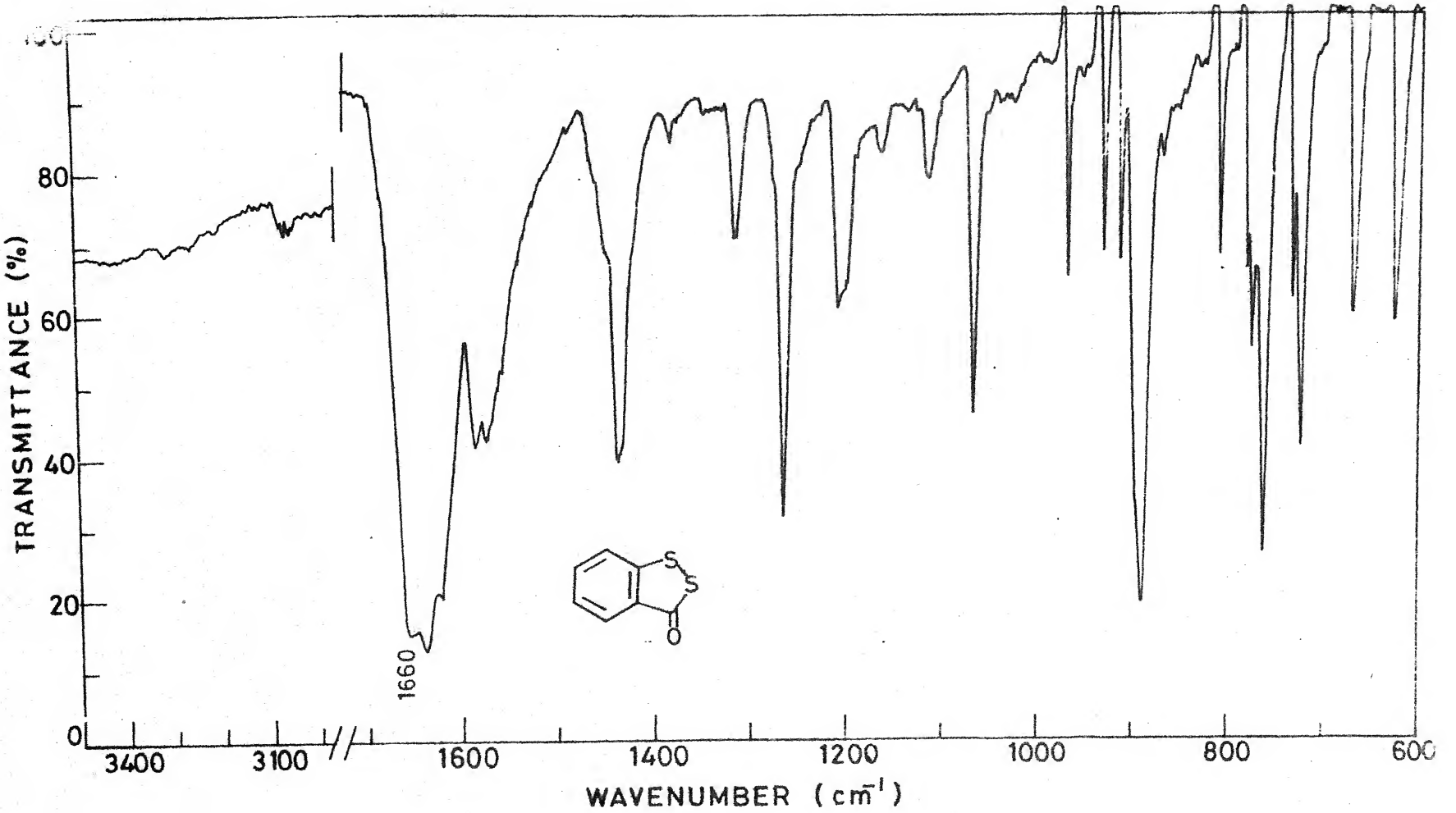
It is interesting to note that ceric ammonium nitrate reacts with various substituted 4-phenyl-Δ'-[1,2,4]triazoline-5-thiones to yield the corresponding triazolinones in very good yields. The reaction takes place under mild conditions and in a relatively shorter period of time. These reactions were carried out at ambient temperature. All the triazolinones show a strong carbonyl absorption at around ν1755 cm^{-1} in the infrared spectrum.

Literature survey revealed that various triazolinones (A) have been prepared by different methods.[44] Thus, for example, A has been synthesized by the reaction of cyclohexanone-4-phenyl semicarbazone, basic alumina and chloroform at room temperature for 7 days. The reaction mixture after filtration, and subsequent chromatography over alumina is reported to furnish the desired product.

Conversion of triazoline thione into triazolinone is achieved[44] by reacting the thione with mercuric acetate in presence of ethanol.

Thus, reaction of CAN with triazoline-5-thiones, provides a versatile substitute for the preparation of triazolinones. The products obtained were characterized by comparison with authentic samples, m.p., IR, ^1H NMR and mass spectra.


S
S
O
AROMATIC
TMS
9.0
8.0
7.0
0
PPM (δ)

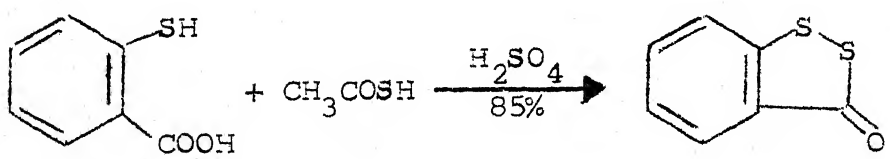

TRANSMITTANCE (%)
0
20
40
60
80
100
3400
3100
1660
1600
1400
1200
1000
800
600
WAVENUMBER (cm⁻¹)
S
S
O

168(M+)
140
136
104
76
28
140
110
90
70
50

Ceric ammonium nitrate reacts with various substituted 3H-1,2-benzodithiole-3-thiones to yield 3H-1,2-benzodithiole-3-ones in excellent yields. These reactions were carried out at room temperature. All benzodithiole-3-ones showed the carbonyl absorption signal located at ν1660 cm^{-1} in the infrared spectrum.

Literature survey revealed[45] that a variety of methods are available for the preparation of 3H-1,2-benzodithiole-3-ones. Smiles and McClelland[46] for example, prepared benzodithiole-3-ones from 2-thiobenzoic acid or 2,2'-dithiobenzoic acid and a disulfide or mercaptan in concentrated sulfuric acid. By adding a mixture of 2-thiobenzoic acid and thioacetic acid to concentrated sulfuric acid McClelland, Warren and Jackson[47] obtained the compound in 85% yield.

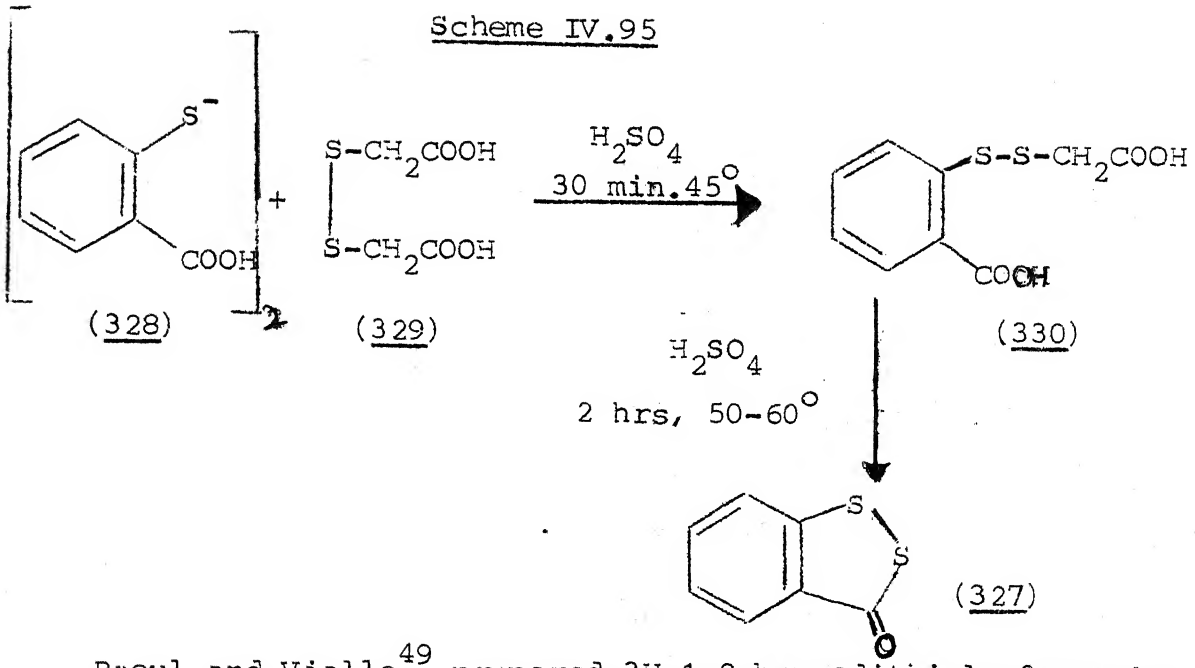
Scheme IV.94



(326) (327)

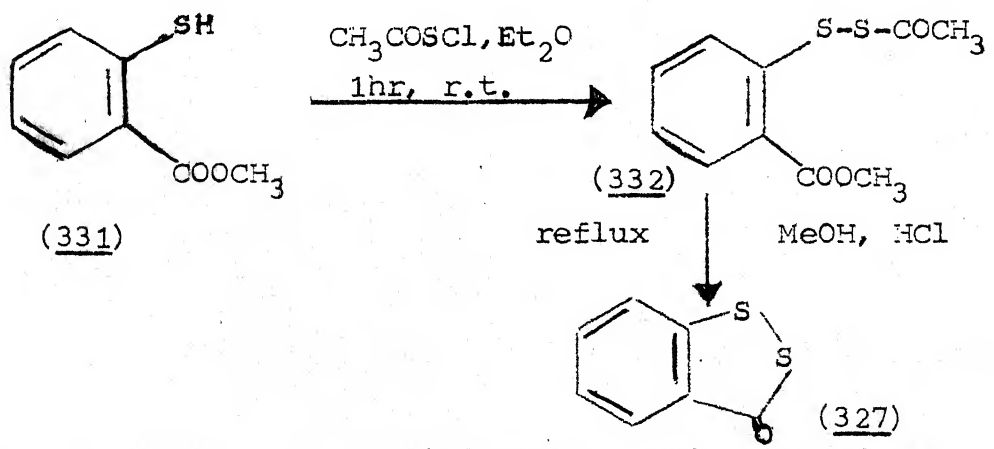
The reaction also succeeded with dithioglycollic acid, hydrogen sulfide, phthalyl sulfide,[46] and ethyl mercaptan.[48] Smiles and McClelland[46] postulated that the reaction is proceeding *via* the formation of the mixed disulfide.

Scheme IV.95

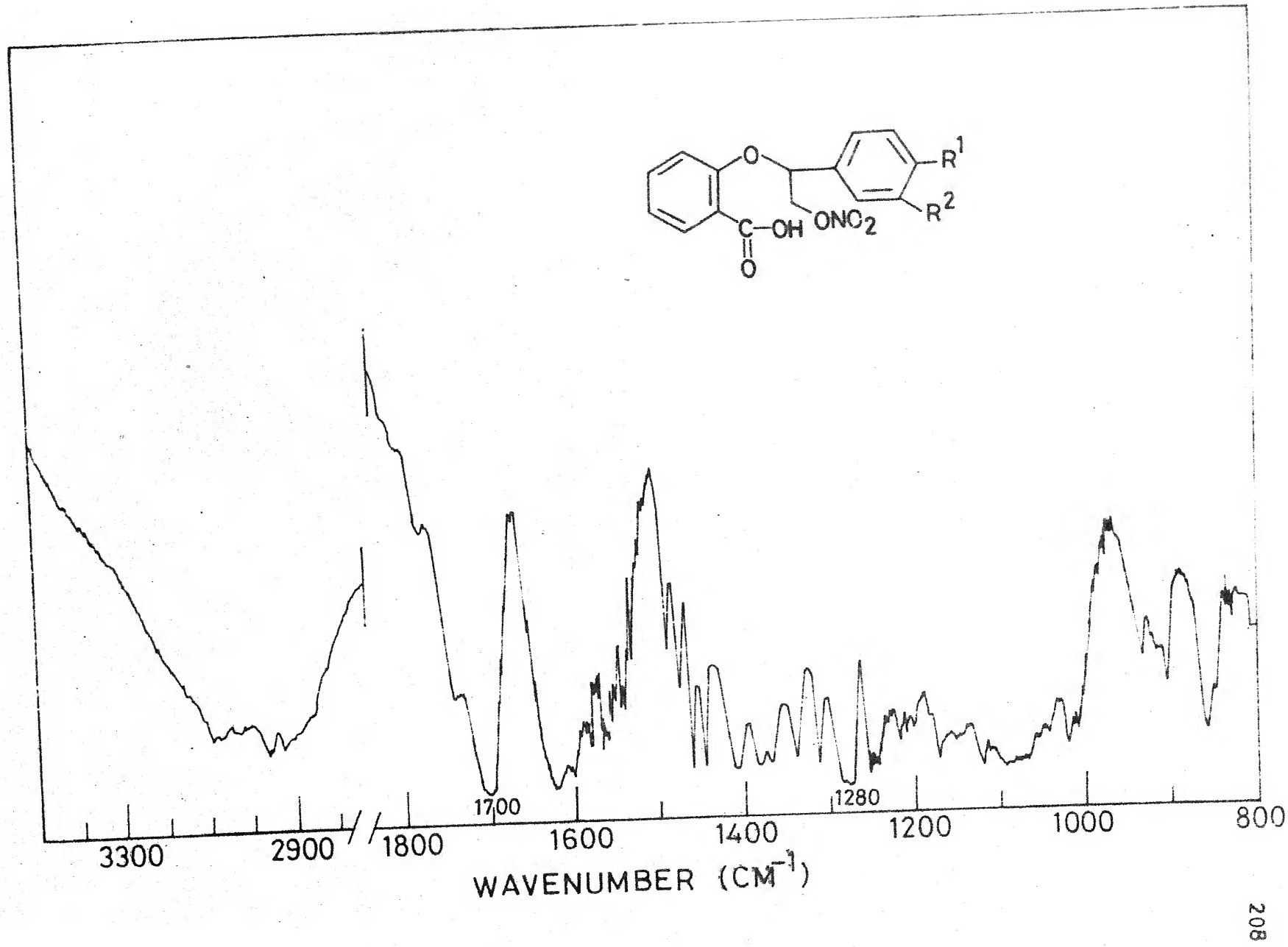


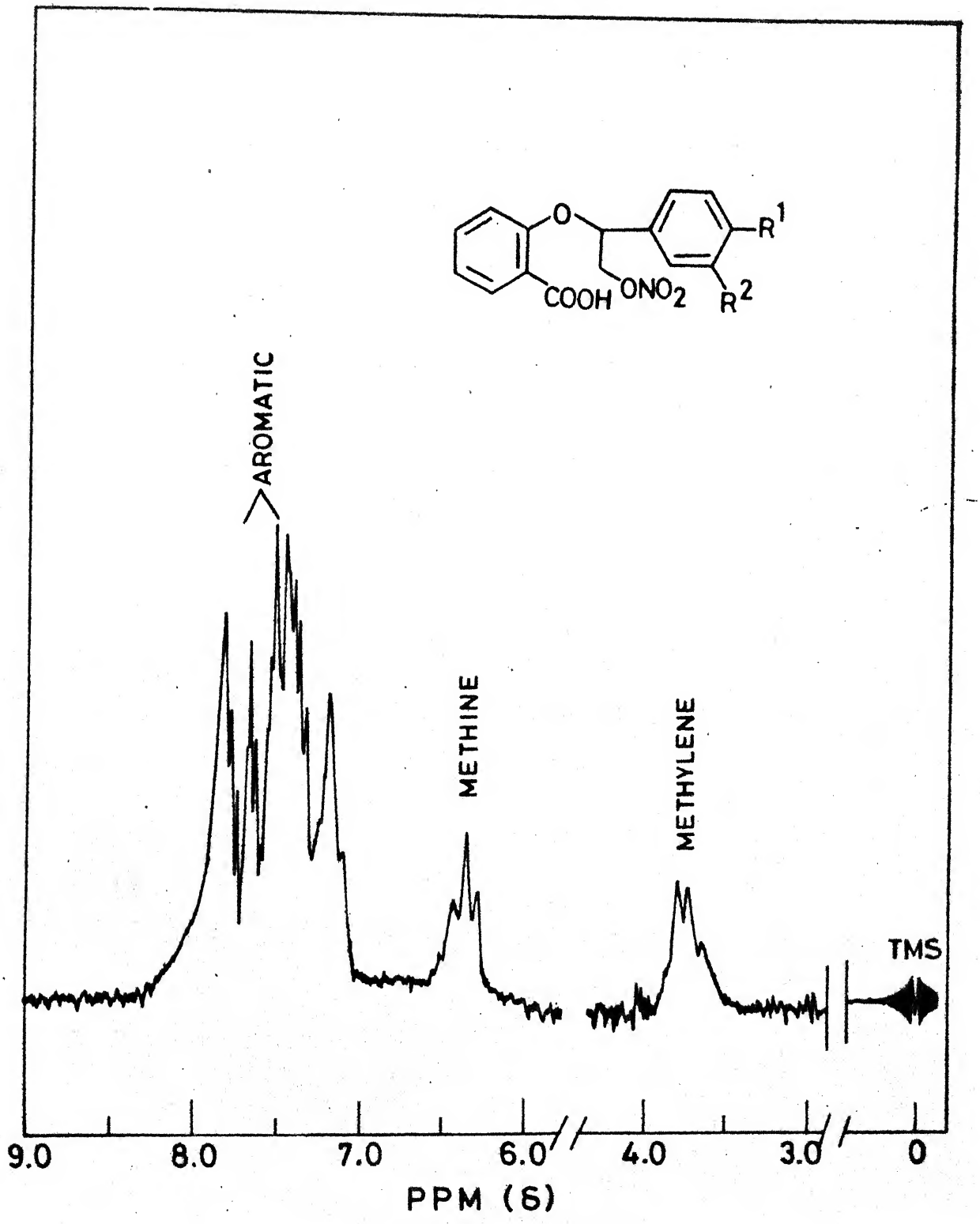
Raoul and Vialle[49] prepared 3H-1,2-benzodithiole-3-one by condensing methyl thiosalicylate with acetylsulfenyl chloride, followed by ring closure with hydrogen chloride.

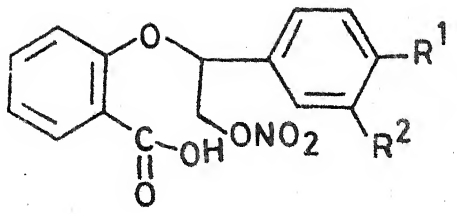
Scheme IV.96

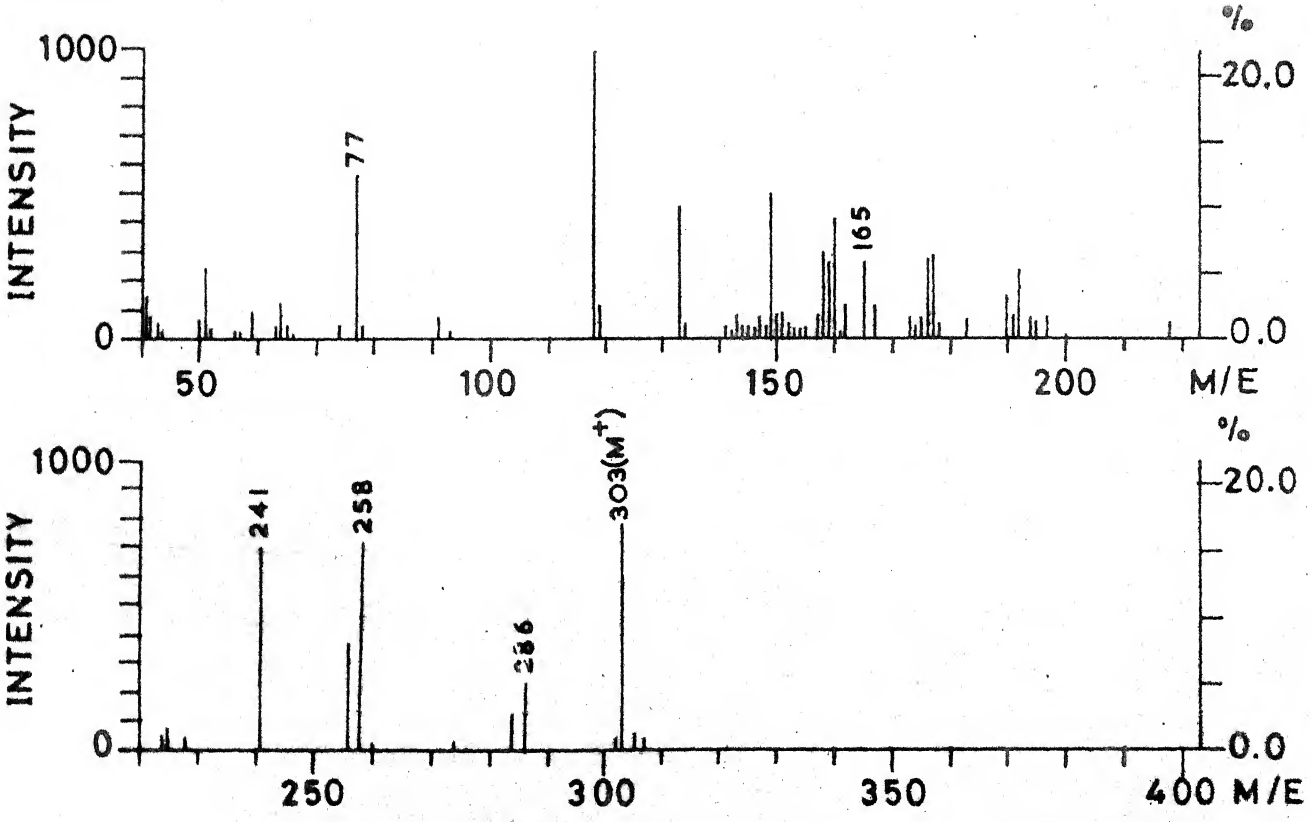


The reactions were carried out by adding 3 equivalents of ceric ammonium nitrate to a stirred solution of various substituted 3H-1,2-benzodithiole-3-thiones (1 equivalent) at 0°. The


O
R1
R2
C
OH
ONO2
O
3300
2900
1800
1700
1600
1400
1280
1200
1000
800
WAVENUMBER (CM-1)


O
R1
COOH
ONO2
R2
AROMATIC
METHINE
METHYLENE
TMS
9.0
8.0
7.0
6.0
4.0
3.0
0
PPM (δ)


O
R1
C
OH
ONO2
R2
O


%
1000
INTENSITY
77
165
20.0
0
0.0
50
100
150
200
M/E
%
1000
INTENSITY
241
258
256
303(M+)
20.0
0
0.0
250
300
350
400 M/E

acid group. Absorption band located at ν1280 cm^{-1} indicates the presence of O-NO_2 moiety in the product. The PMR spectrum shows a multiplet δ7.1-8.0 of aromatic protons. The methine proton shows up as a peak at δ6.3, as a triplet. The protons appear at lower field because -CH proton is sandwiched between phenyl and the oxygen atom. The methylene protons appear at δ3.7, as a doublet. The assigned structure is supported by its mass spectral data.

EXPERIMENTAL

All the melting points are uncorrected and were taken on Fischer-Johns melting point apparatus. The specification of the IR, NMR and Mass spectrometers were the same as described earlier (vide Chapter 1). A B.D.H. sample of ceric ammonium nitrate was employed for carrying out the oxidation reactions.

Preparation of 3H-1,2-Benzodithiole-3-thione:

2,2'-Dicarboxydiphenyl disulfide: To the stirred solution of Na_2S_2, an ice-salt cooled solution of diazotised anthranilic acid was added dropwise (0.5 h). The diazotised anthranilic acid was prepared by slow addition of aqueous $NaNO_2$ (8.2g, 35 ml) to an ice-salt cooled, stirred solution of anthranilic acid (16g) in conc. HCl (25 ml). The reaction mixture was allowed to attain room temperature and stirred till N_2 evolution ceased, acidified with conc. HCl, filtered and washed with water. This was then mixed with 5% Na_2CO_3 (500ml), refluxed and filtered hot over sulfur,

filtered and dried to give 2,2'-dicarboxy diphenyl disulfide (16g, 90%), m.p., 288° (lit. 290°).

A mixture of phosphorus pentasulfide (5g), 2,2'-dicarboxy diphenyl disulfide (5g) and xylene (115 ml) was refluxed for 6 h. It was subjected to steam distillation to remove xylene. The residue washed with water, filtered and crystallised from ethanol to give 2,3-dithio sulfindene (4.5g, 75%), m.p., 92° (lit. 94°).

Reaction of 4-phenyl-Δ'-[1,2,4]triazoline-5-thiones with CAN (General Method):

To a stirred solution of 4-phenyl-Δ'-[1,2,4]triazoline-5-thione (0.001 mol) in acetonitrile (6 ml) was added CAN (2.192g, 0.001 mol) in water (6 ml). The reaction was continued for an additional 30 minutes. The reaction mixture was saturated with NaCl, extracted with ether (3x10 ml). Removal of the solvent gave the titled product. It was purified by crystallisation (Benzene petroleum ether, 1:1). The yields and melting points of the compounds prepared in this manner are listed in Table-1.

Reaction of 3H-1,2-Benzodithiole-3-thiones with CAN (General Method):

CAN (3.27g, 0.003 mol) in water (6 ml) was added to a stirred solution of 3H-1,2-benzodithiole-3-thione (0.001 mol) in acetonitrile (5 ml). As soon as the reaction was complete (TLC monitoring), the reaction mixture was saturated with NaCl, extracted with

ether (3x10 ml). Removal of the solvent gave the residue. The resulting material was chromatographed on a silica gel column and eluted with benzene. Evaporation of the solvent afforded the pure compounds. The yields and melting points of the compound thus prepared are listed in Table-2.

Oxidative cleavage of Flavanones with CAN (General Method):

To a stirred solution of flavanone (0.001 mol), was added CAN (0.008 mol) in aqueous acetonitrile at room temperature. The reaction mixture was then allowed to reflux for an additional 3 h, on a water-bath. After the completion of the reaction (as monitered by tlc) the reaction mixture was extracted with ether, dried over Na_2SO_4. After the solvent was evaporated off, the residue was chromatographed (Benzene, silica gel) to afford the corresponding products. The yields and melting points of the compounds thus prepared are listed in Table- .

Reaction of 4-phenyl-Δ'-[1,2,4]triazoline-5-thiones with pyridinium chlorochromate (PCC) (General Method):

To a stirred mixture of 5(a-j) (0.001 mol) was added PCC (0.862g, 0.004 mol) at room temperature. The reaction mixture was stirred for 3 h, diluted with dry ether and filtered through a pad of silica gel. The filtered cake was washed thoroughly with ether and the combined filtrate was concentrated to get a residue. It

TABLE-1

Δ²-[1,2,4]triazoline-5-ones

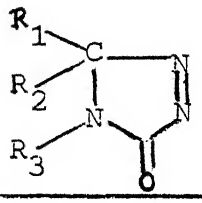
Compound No. (332)		Yield (%)	M.pt.(°C) observed	M.pt.(°C) literature
a	$R_1=R_2=CH_3$, $R_3=C_6H_5$	95	143	144
b	$R_1=CH_3$, $R_2=C_2H_5$, $R_3=C_6H_5$	92	120	122
c	$R_1,R_2= -(CH_2)_5-$, $R_3=C_6H_5$	85	180	185
d	$R_1,R_2= -(CH_2)_4-$, $R_3=C_6H_5$	89	160	162
e	$R_1=R_2=C_2H_5$, $R_3=C_6H_5$	85	150	151
f	$R_1=R_2=CH_3$, $R_3=$p-ClC_6H_4	93	130	131
g	$R_1=CH_3$, $R_2=C_2H_5$, $R_3=$p-ClC_6H_4	90	87	88
h	$R_1,R_2= -(CH_2)_5-$, $R_3=$p-ClC_6H_4	87	200	202
i	$R_1,R_2= -(CH_2)_4-$, $R_3=$p-ClC_6H_4	86	168	170
j	$R_1=R_2=C_2H_5$, $R_3=$p-ClC_6H_4	88	170	172

TABLE-2

3H-1,2-Benzodithiole-3-ones

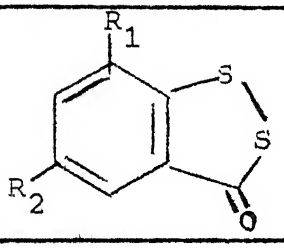
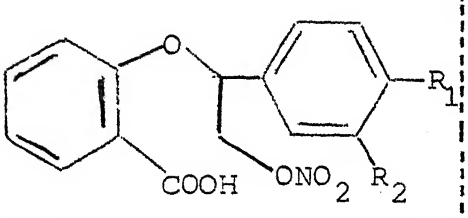
Compound No. (327)		Yield (%)	M.Pt(°C)	
			observed	literature
a	$R_1=R_2=H$	96	74	76
b	$R_1=H$, $R_2=CH_3$	93	78	77
c	$R_1=CH_3$, $R_2=H$	90	89	90
d	$R_1=R_2=Cl$	85	112	114
e	$R_1=H$, $R_2=Cl$	80	110	111

TABLE-3

Compound No. (333)		Yield (%)	M.Pt(^{o}C)
a	$R_1=R_2=H$	70	132
b	$R_1=OCH_3$, $R_2=H$	68	141
c	$R_1=CH_3$, $R_2=H$	72	138
d	$R_1=R_2=OCH_3$	74	152

was purified by crystallization from Benzene:Petroleum ether (1:1). Yield 75%, spectral data and m.p. identical with that obtained in the oxidation with CAN.

Synthesis of (332a)	:	Yield: 0.179g (95%), m.p. 143°.
Calcd analysis for $C_{10}H_{11}N_3O$	:	C: 63.40; H: 5.82; N: 22.20
Found	:	C: 63.12; H: 5.98; N: 22.00%
IR spectrum (KBr) ν_{max}	:	1750 ($\nu_{C=O}$) cm^{-1}.
PMR spectrum ($CDCl_3$), δ ppm	:	1.6 (s, 6H, CH_3), 7.0-7.8 (m, 5H, aromatic).
Mass spectrum	:	m/z: 189 (M^+).
Synthesis of (332b)	:	Yield: 0.192g (92%), m.p. 120°.
Calcd analysis for $C_{11}H_{13}N_3O$	:	C: 65.02; H: 6.40; N: 20.6
Found	:	C: 64.90; H: 6.52; N: 19.1%
IR spectrum (KBr) ν_{max}	:	1755 ($\nu_{C=O}$) cm^{-1}.
PMR spectrum ($CDCl_3$), δ ppm	:	1.6 (s, 3H, CH_3), 1.8 (t, 3H, CH_3), 2.4 (q, 2H, CH_2), 7.2-7.5 (m, 5H, aromatic).
Mass spectrum	:	m/z: 203 (M^+).

Synthesis of (332c) : Yield: 0.194g (85%), m.p. 180°.

Calcd analysis for $C_{13}H_{15}N_3O$: C: 68.12; H: 6.55; N: 18.34

Found : C: 68.01; H: 6.42; N: 18.20%

IR spectrum (KBr) ν_{max}: : 1750 ($\nu_{C=O}$) cm^{-1}.

PMR spectrum ($CDCl_3$), δ ppm : 1.7 (m, 10H, $-CH_2-$), 7.0-7.5 (m, 5H, aromatic).

Mass spectrum : m/z: 229 (M^+).

Synthesis of (332d) : Yield: 0.191g (89%), m.p. 160°.

Calcd analysis for $C_{12}H_{13}N_3O$: C: 66.9; H: 6.04; N: 19.53

Found : C: 66.71; H: 6.21; N: 19.62%

IR spectrum (KBr) ν_{max} : 1755 ($\nu_{C=O}$) cm^{-1}.

PMR spectrum ($CDCl_3$), δ ppm : 1.6 (m, 8H, $-CH_2-$), 7.5-7.8 (m, 5H, aromatic).

Mass spectrum : m/z: 215 (M^+).

Synthesis of (332e) : Yield: 0.184g (85%), m.p. 150°.

Calcd analysis for $C_{12}H_{15}N_3O$: C: 66.3 ; H: 6.91; N: 19.35

Found : C: 66.19; H: 6.80; N: 19.49%

IR spectrum (KBr) ν_{max} : 1755 ($\nu_{C=O}$) cm^{-1}.

PMR spectrum ($CDCl_3$), δ ppm : 1.8 (t, 6H, CH_3), 2.3 (q, 4H, $-CH_2$), 7.0-7.6 (m, 5H, aromatic).

Mass spectrum : m/z: 217 (M^+).

Synthesis of (332f) : Yield: 0.207g (93%), m.p. 130°.

Calcd analysis for $C_{10}H_{10}ClN_3O$: C: 53.81; H: 4.48; N: 18.83

Found : C: 53.70; H: 4.59; N: 18.95%

IR spectrum (KBr) ν_{max} : 1750 ($\nu_{C=O}$) cm^{-1}.

PMR spectrum ($CDCl_3$), δppm : 1.8 (s, 6H, CH_3), 7.2-7.8 (m, 4H, aromatic).

Mass spectrum : m/z: 223 (M^+).

Synthesis of (332g) : Yield: 0.213g (90%), m.p. 87°.

Calcd analysis for $C_{11}H_{12}ClN_3O$: C: 55.69; H: 5.06; N: 17.72

Found : C: 55.52; H: 5.22; N: 17.62%

IR spectrum (KBr) ν_{max} : 1750 ($\nu_{C=O}$) cm^{-1}.

PMR spectrum ($CDCl_3$), δ ppm : 1.6 (s, 3H, CH_3), 1.8 (t, 3H, CH_3), 2.3 (q, 2H, CH_2), 7.6-8.0 (m, 4H, aromatic).

Mass spectrum : m/z: 237 (M^+).

Synthesis of (332h) : Yield: 0.228g (87%), m.p. 200°.

Calcd analysis for $C_{13}H_{14}ClN_3O$: C: 59.31; H: 5.32; N: 15.96

Found : C: 59.45; H: 5.25; N: 15.80%

IR spectrum (KBr) ν_{max} : 1755 ($\nu_{C=O}$) cm^{-1}.

PMR spectrum ($CDCl_3$), δ ppm : 1.6 (m, 10H, $-CH_2$), 7.6-8.0 (m, 4H, aromatic).

Mass spectrum : m/z: 263 (M^+).

Synthesis of (332i) : Yield: 0.227g (86%), m.p. 168°.

Calcd analysis for $C_{12}H_{12}ClN_3O$: C: 57.83; H: 4.81; N: 16.86

Found : C: 57.68; H: 4.99; N: 16.73%

IR spectrum (KBr) ν_{max} : 1755 ($\nu_{C=O}$) cm^{-1}.

PMR spectrum ($CDCl_3$), δ ppm : 1.7 (m, 8H, $-CH_2-$), 7.2-7.8 (m, 4H, aromatic).

Mass spectrum : m/z: 265 (M^+).

Synthesis of (332j) : Yield: 0.220g (88%), m.p. 170°.

Calcd analysis for $C_{12}H_{14}ClN_3O$: C: 57.37; H: 5.57; N: 16.73

Found : C: 57.21; H: 5.69; N: 16.50%

IR spectrum (KBr) ν_{max} : 1750 ($\nu_{C=O}$) cm^{-1}.

PMR spectrum ($CDCl_3$), δ ppm : 1.8 (t, 6H, CH_3), 2.2 (q, 4H, CH_2), 7.0-7.5 (m, 4H, aromatic).

Mass spectrum : m/z: 251 (M^+).

Synthesis of (327a) : Yield: 0.161g (96%), m.p. 74°.

Calcd analysis for $C_7H_4S_2O$: C: 50.0; H: 2.38;

Found : C: 48.1; H: 2.46%

IR spectrum (KBr) ν_{max} : 1660 ($\nu_{C=O}$) cm^{-1}.

PMR spectrum ($CDCl_3$), δ ppm : 7.2-7.8 (m, 4H, aromatic).

Mass spectrum : m/z: 168 (M^+).

Synthesis of (327b) : Yield: 0.169g (93%), m.p. 78°.

Calcd analysis for $C_8H_6S_2O$: C: 52.74; H: 3.29

Found : C: 52.65; H: 3.04%

IR spectrum (KBr) ν_{max} : 1665 ($\nu_{C=O}$) cm^{-1}.

PMR spectrum ($CDCl_3$), δ ppm : 2.2 (s, 3H, CH_3), 7.1-8.0 (m, 3H, aromatic).

Mass spectrum : m/z: 182 (M^+).

Synthesis of (327c) : Yield: 0.163g (90%), m.p. 89°.

Calcd analysis for $C_8H_6S_2O$: C: 52.74; H: 3.29

Found : C: 52.67; H: 3.08%

IR spectrum (KBr) ν_{max} : 1655 ($\nu_{C=O}$) cm^{-1}.

PMR spectrum ($CDCl_3$), δ ppm : 2.1 (s, 3H, CH_3), 7.3-7.6 (m, 3H, aromatic).

Mass spectrum : m/z: 182 (M^+).

Synthesis of (327d) : Yield: 0.201g (85%), m.p. 112°.

Calcd analysis for $C_7H_2Cl_2S_2O$: C: 35.44; H: 0.84

Found : C: 35.36; H: 1.01%

IR spectrum (KBr) ν_{max} : 1655 ($\nu_{C=O}$) cm^{-1}.

PMR spectrum ($CDCl_3$), δ ppm : 7.3-7.4 (t, 2H, aromatic).

Mass spectrum : m/z: 237 (M^+).

Synthesis of (327e) : Yield: 0.161g (80%), m.p. 110°.

Calcd analysis for $C_7H_3ClS_2O$: C: 41.58; H: 1.48

Found : C: 41.42; H: 1.57%

IR spectrum (KBr) ν_{max} : 1660 ($\nu_{C=O}$) cm^{-1}.

PMR spectrum ($CDCl_3$), δ ppm : 7.4-7.6 (m, 3H, aromatic).

Mass spectrum : m/z: 202 (M^+).

Synthesis of (333a) : Yield: 0.212g (70%), m.p. 132°.

Calcd analysis for $C_{15}H_{13}NO_6$: C: 59.40; H: 4.29; N: 4.62

Found : C: 59.31; H: 4.41; N: 4.58%

IR spectrum (KBr) ν_{max} : 1700 ($\nu_{C=O}$), 1280 (ν_{O-NO_2}) cm^{-1}.

PMR spectrum ($CDCl_3$), δ ppm : 3.7 (d, 2H, $-CH_2$), 6.3 (t, 1H, -C-H), 7.0-8.0 (m, 9H, aromatic).

Mass spectrum : m/z: 303 (M^+).

Synthesis of (333b) : Yield: 0.226g (68%), m.p. 141°.

Calcd analysis for $C_{15}H_{12}NO_6$: C: 54.05; H: 3.60; N: 4.20

Found : C: 53.83; H: 3.21; N: 4.11%

IR spectrum (KBr) ν_{max} : 1710 (ν C=O), 1270 (ν O-NO_2) cm^{-1}.

PMR spectrum ($CDCl_3$), δ ppm : 3.6 (d, 2H, $-CH_2$), 3.8 (s, 3H, OCH_3), 6.4 (t, 1H, -C-H), 7.1-7.6 (m, 8H, aromatic).

Mass spectrum : m/z: 333 (M^+).

Synthesis of (333c) : Yield: 0.228g (72%), m.p. 138°.

Calcd analysis for $C_{16}H_{15}NO_6$: C: 60.50; H: 4.73; N: 4.41

Found : C: 60.39; H: 4.81; N: 4.20%

IR spectrum (KBr) ν_{max} : 1700 ($\nu_{C=O}$), 1285 (ν_{O-NO_2}) cm^{-1}.

PMR spectrum ($CDCl_3$), δ ppm : 1.6 (s, 3H, CH_3), 3.8 (d, 2H, -C-H), 6.3 (t, 1H, -C-H), 7.1-7.7 (m, 8H, aromatic).

Mass spectrum : m/z: 317 (M^+).

Synthesis of (333d) : Yield:0.268g(74%), m.p. 152°.

Calcd analysis for $C_{17}H_{17}NO_8$: C: 56.19; H: 4.68; N: 3.85

Found : C: 56.02; H: 4.50; N: 3.97%

IR spectrum (KBr) ν_{max} : 1720 ($\nu_{C=O}$), 1275 (ν_{O-NO_2}) cm^{-1}

PMR spectrum ($CDCl_3$), δ ppm : 3.5 (d, 2H, $-CH_2$), 3.7 (s, 6H, OCH_3), 6.5 (t, 1H, -C-H), 7.0-7.6 (m, 8H, aromatic).

Mass spectrum : m/z: 363 (M^+).

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